France Greffe de Moelle
French Registry of unrelated stem cell donors

Agence de la biomédecine

Operations manual

April 2023

Glossary

ABM : Agence de la Biomédecine

ANSM : Agence Nationale de Sécurité du Médicament et des produits de santé
(The national Agency for drug and health product safety)

ARS : Agence Régionale de Santé (The Regional Health Agency)

CHU : Center Hospitalier Universitaire (University Hospital Center)

CMS : Comité Médical et Scientifique (Medical and Scientific Council)

CSH : Cellules Souches Hématopoïétiques (Hematopoietic Stem Cell)

DG : Directeur Général (General Director)

DGS : Direction Générale de la Santé (Direction of the Ministry of Solidarity and Health)

DGOS : Direction Générale de l'Offre de Soins (General Direction of Health Care Supply)

DPG-CSH : Direction du Prélèvement et des Greffes de Cellules Souches Hématopoïétiques (Hematopoietic Stem Cell Transplant Department)

EFS : Etablissement Français du Sang (The French Blood Establishment)

EMDIS : European Marrow Donor Information System

ES : Etablissement de Santé (Health Care Center)

FGM : France Greffe de Moelle (Stem Cell Donor Registry)

HAS: Haute Autorité de Santé (The French National Authority for health)

RFSP : Réseau Français de Sang Placentaire (French Cord Blood Network)

RNCD : Réseau National des Centers Donneurs (National Network of Donor Centers)

SYRENAD : Système de Recherche National des Donneurs (National Donor Search System)

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1. The French unrelated stem cell donor registry: organization and interactions

Created in 1986, the French unrelated stem cell donor registry (France Greffe de Moelle, hereafter FGM) is responsible for managing the national volunteer bone marrow donors panel, the national cord blood units inventory, and the national and international patients registration for an unrelated donor search or an hematopoietic stem cell (HSC) transplant. It coordinates these searches and the organization of HSC collection from donors and cord blood unit shipments as requested by national or international Transplant Centers (hereafter TCs).

The FGM registry is the mandatory interface between TCs, Donor Centers (hereafter DCs), and international registries. It guarantees perfect donor/recipient anonymity and facilitates the organization of searches for donors both in France and internationally.

This registry works in close collaboration with both internal and external partners to promote bone marrow donations, recruit new donors, and manage the national donor panel.

Since 2006, the FGM registry is part of the Agence de la biomedecine (hereafter ABM), a public administrative establishment overseen by the ministry of health, which reports its activity and its application of the law to Parliament and the Government (Public Health Code article L. 1418-1).

1.1. Agence de la biomedecine — Missions and strategic objectives

The ABM oversees, supervises, supports, and assesses activities in the domains of the transplantation of organs, tissues, and cells, as well as in the areas of human reproduction, embryology, human genetics, embryo research, and human embryonic stem cell research. It simultaneously performs missions involving training, expertise, and operations.

The ABM organizes its activity around major strategic orientations related to:

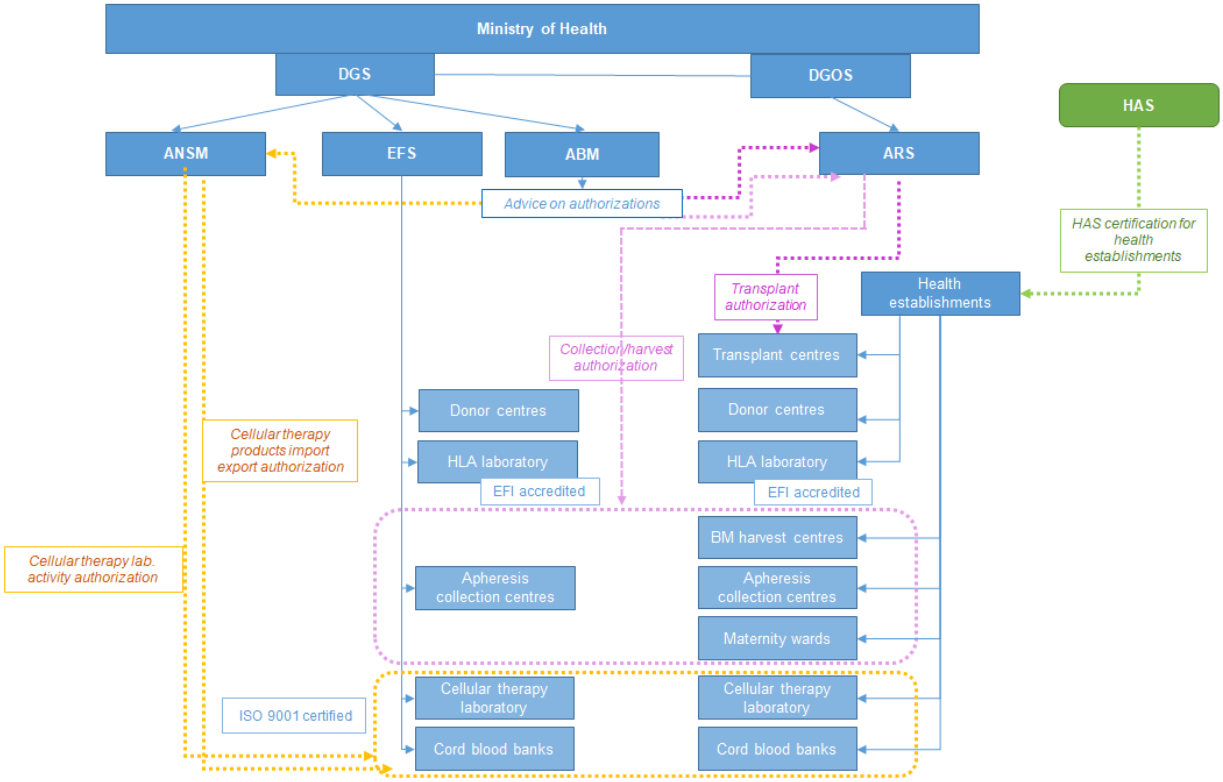
- contributing to public health, performance, and efficiency, in association with its institutional partners (supervising authorities, the agency system, and the regional health agencies), in accordance with a contract of objectives and performance (COP) — a strategic document intended to put into writing its contractual obligations to the State related to these major orientations
- Increasing the number and quality of the biological substances collected and transplanted, accessing all sources of grafts necessary to meet patients' needs, in accordance with the HSC transplantation ministerial five-year plan developed in partnership with all of the stakeholders concerned — professional societies, associations, and organizations representing healthcare professionals…

1.2. The ABM's institutional partners

The ABM is part of the French network connecting experts and professionals in the fields of health, science, and medicine. It works in close collaboration with other health institutions (health agencies, regional health agencies, and other bodies) on numerous public health topics, under the direction of the ministry of solidarity and health (DGS, DGOS) – Fig.1.

It is also involved in issuing authorization and accreditation for healthcare facilities; the regional health agencies (ARS) ask for ABM Notice of Authorization before authorizing HSC collection and transplantation by facilities, as does the national drug and health product safety Agency (ANSM) before authorizing the preparation, storage, and distribution of cell therapy products.

ABM institutional partners involved in HSC collection and transplantation (activity and authorizations)



- **The regional health agencies (ARS)**

The regional health agencies (ARS) are public establishments, morally and financially autonomous, but nonetheless overseen by the ministries of both social affairs and of health. They are responsible for coordinating and overseeing the regional healthcare system. In turn, they define and implement health policy in the region and regulate the healthcare supply.

After receiving the ABM's advice, these ARS authorize establishments to collect and to transplant the HSCs collected in bone marrow or blood and intended for making cell therapy preparations, in application of article L. 1243-2, in accordance with "Decree no. 2007-519 dated April 5, 2007, concerning the conditions for the authorization of cell collection activity, modifying the Public Health Code (regulatory provisions)".

- **The national Agency for drug and health product safety (ANSM)**

The ANSM is a public establishment overseen by the ministry of health. Its jurisdiction includes drugs and their raw materials, medical devices, and medical devices for in vitro diagnosis, biological products of human origin (labile blood products, organs, tissue, cells, products for gene and cell therapy), and related therapeutic products as well as cosmetic products.

The ANSM is responsible for assessing the benefits and risks associated with the use of health products throughout their life cycles. It evaluates the safety, efficacy, and quality of these products and their use. It ensures their laboratory monitoring and control and in particular inspects their manufacturing sites.

After receiving the ABM's technical advice, the ANSM authorizes the national cell therapy units/laboratories associated with collection centers, transplantation centers, and cord blood banks to perform activities for the preparation, storage, distribution, and transfer of the cells and cell therapy preparations, as called for by Public Health Code article L.1243-2.

- **The National Authority for Health (HAS)**

The French national authority for health (HAS) is an independent public authority, of a scientific nature. Its tasks are to assess health products to determine if and how much they should be reimbursed, to recommend good practice guidelines for professionals working in health, social services, and medical-social areas, to recommend public health policies, and to measure and improve the quality of care in hospitals and clinics and of support in social and medical-social establishments.

In particular, it is responsible for the certification of hospitals and clinics.[1] Certification is a system of external assessment that is required for every healthcare facility, public or private, regardless of its size and activity. It is conducted every 4 to 6 years by professionals appointed by the HAS to provide an independent assessment of the establishment (and its supervisory bodies) in terms of the level of services and care delivered to patients and the process of improving the quality and safety of its care.

- **The French blood establishment (EFS)**

The French blood establishment is a public establishment of the State overseen by the minister of health. It is the unique civil blood transfusion operator in France; its mission is to ensure the self-sufficiency of France in blood products in optimal conditions of safety and quality.

Donor centers, collection centers, and storage banks for cord blood grafts belonging to the EFS ensure the management of all stages from the enrolment of donors, the eventual collection of their blood, and their follow-up, as well as the management of the storage of cord blood for transplantation.
The collaboration between the ABM and the EFS is governed by an agreement renewable every 4 years.

1.3. The place of the FGM registry at the ABM

The FGM registry is a branch of the HSC collection and transplant division (DPG-HSC), one of the ABM's three medical and scientific divisions (see the Fig. 2: functional organizational chart). It groups together the activities associated with HSC donation, collection, and transplantation, with as a major objective to contribute to developing and facilitating access to HSC transplants for an increasing number of patients.

The DPG-HSC has three branches:

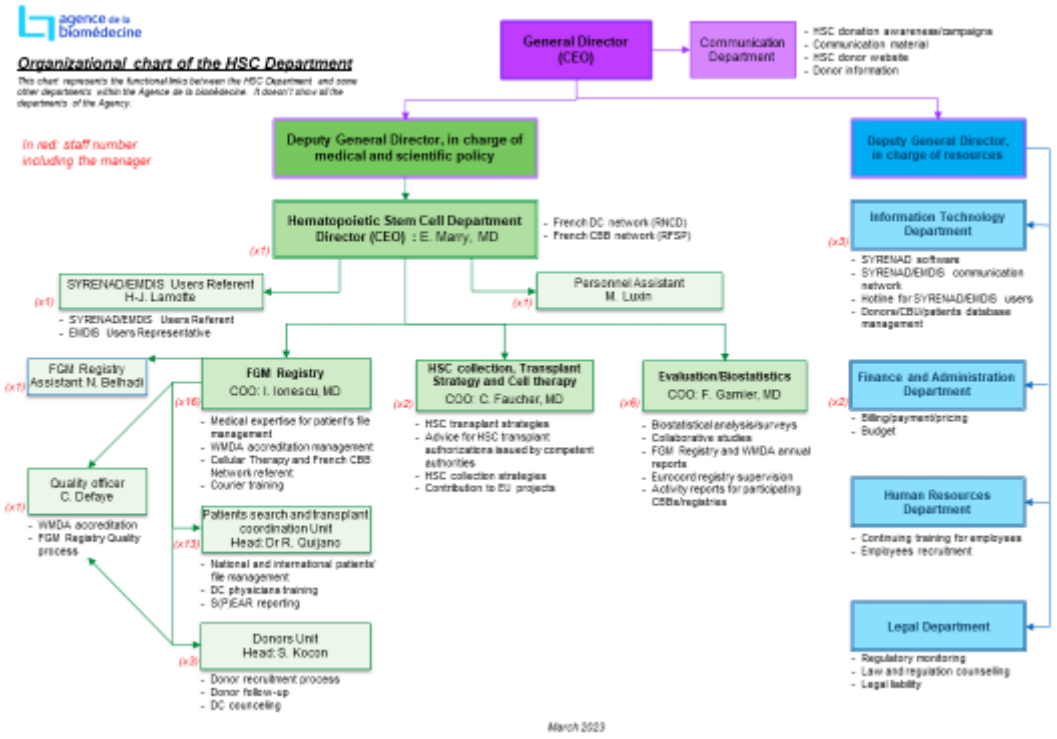
- The FGM registry, that is, the national registry that manages donors, cord blood units, and national and international patients and organizes the donor searches, the collection of cord blood/stem cells, and transplantation of unrelated allografts;

- The HSC collection and transplant strategy department, which focuses on the strategy deployed around the collection, transplantation, and cell therapy linked to HSCs. It is also responsible for administering opinions about authorizations and for following up the progress of the ministerial five-year plan for the collection and transplantation of HSC;

- The assessment-biostatistics department which brings together the activities of statistical analysis and evaluation from three separate databases: Syrenad (national donor research system), EDMA (Eurocord Data Management Assistant) and EBMT-Promise.

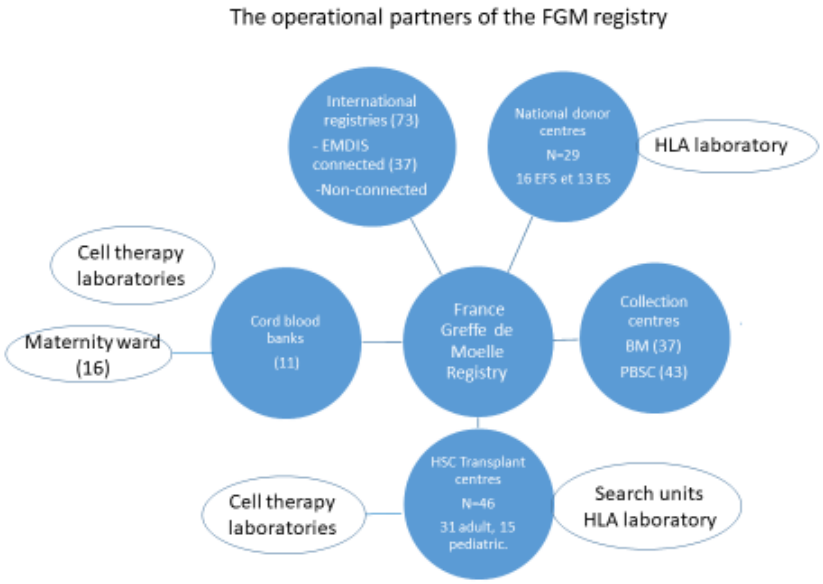
The FGM registry also receives support from the ABM's resource divisions, in particular, those of communication, of administration and finance, and of information systems; all of these contribute cross-sectionally to the FGM registry's missions.
The FGM registry puts together a complete annual activity report that allows its activity to be analyzed and its trends to be monitored.

[1] Public Health Code Articles L. 6113-3 et seq.



1.4. The operational partners of the French stem cell donor registry (FGM)

The FGM registry's work relies on the close daily collaboration of a network made up exclusively of entities declared qualified by the relevant authorities:



- **Donor centers:**

  A donor center (DC) relies on a histocompatibility laboratory (HLA) which is EFI accredited or which has concluded an agreement with an EFI accredited laboratory. This laboratory belongs either to the French blood authority (EFS) or to a hospital (ES).

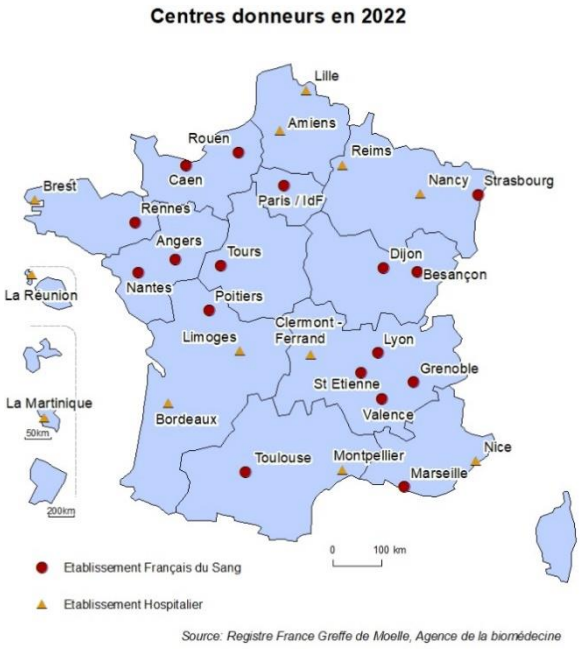
  DCs perform, on behalf of the ABM, the recruitment, registration, and management of unrelated HSC donors, relying on a histocompatibility laboratory responsible for typing the donors' HLA, from registration through the final selection of a compatible donor.
  This histocompatibility laboratory must be accredited by the European Federation of Immunogenetics (EFI) or must have a contract of collaboration with such an EFI-accredited laboratory.

  Auxiliary centers can be affiliated with a donor center. Their role is to receive volunteers for registration or for a blood sample draw for additional typing, at the request of the donor center.

  The DC is part of the national network of donor centers (RNCD), a network created by the ABM to help accomplish its task of administering the FGM Registry. This network federates the 29 donor centers working with the FGM registry, and relies on their field experience and expertise to propose new strategic orientations for bone marrow donation.

  The DC must comply with the World Marrow Donor Association (WMDA) quality standards. The FGM registry evaluates this compliance each year in relation to the center's activities, including those of its auxiliary centers.

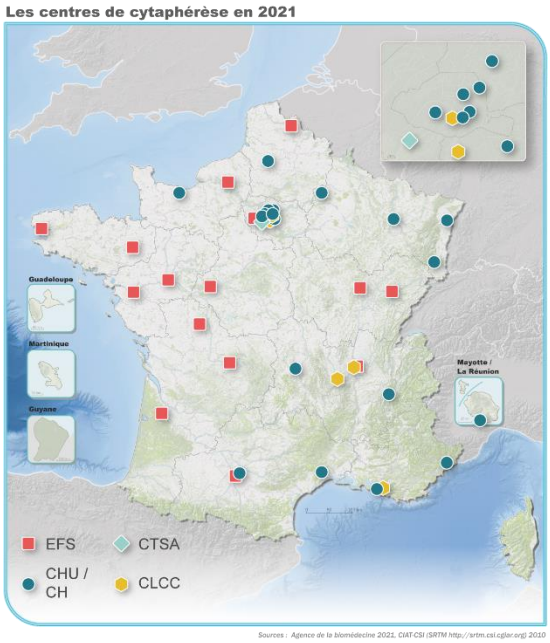
  National donor centers - 2022



Source: Registre France Greffe de Moelle, Agence de la biomédecine

- **The HSC collection center:** Allogenic HSC can be collected only in university hospital centers (CHU), cancer centers (CLCC) or EFS local offices, all of which must be specifically authorized to do so by the ARS with jurisdiction over the collection center, after the ABM has expressed its advice.[2] This authorization is valid for 5 years and can be renewed. The list of authorized collection centers, established from information transmitted by the ARS, is available at the ABM website.
  Bone marrow collection is performed exclusively at authorized hospital centers (CHU-CLCC). The apheresis departments for the collection of peripheral stem cells belong either to the EFS or to authorized CHU-CLCCs.
  Each collection center is geographically linked to a specific donor center. The collection centers have a binding agreement with their donor center for the collection of HSCs from recruited donors.

National collection center (apheresis) – 2021



- **The Cell Therapy Laboratory (CTL)** is responsible for the preparation, processing, verification, storage, and distribution of therapy products intended for transplantation — autologous or allogenic. This laboratory operates according to the Good Practice Guidelines for cell therapy (AFSSAPS decision dated October 27, 2010, as modified by the ANSM decision dated May 5, 2017).

  The CTL must be authorized by the ANSM, after receiving the ABM advice, to practice cell therapy activities, as required by Public Health Code article L.1243-2.
  CTLs are affiliated either with the EFS or with an hospital center.

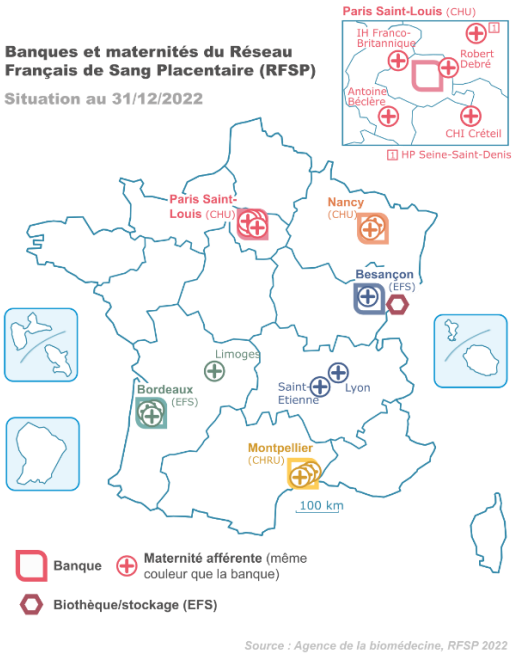
- **Cord blood banks:** A cord blood bank is part of a cell therapy lab and its activities, which involve cell therapy, are authorized by the ANSM.

[2] Public Health Code Article L. 1242-1

All HSC treatments collected from cord blood, from collection to storage, take place in establishments affiliated with the French cord blood network (RFSP), which gathers public cord blood banks and their associated maternities. The main objective is to reach both qualitative and quantitative objectives for cord blood units storage set by the ABM in the framework of the defined ministerial 5-year period plan. The RFSP plays a role in the training of the healthcare professionals concerned and in increasing the awareness of and providing information to pregnant women about cord blood donation. The RFSP is steered by the ABM. The FGM registry collaborates with 5 active cord blood banks, which continue their banking activities to increase the national stock, and with 6 other cord blood banks which now only store and release cord blood units. Each cord blood bank complies with the applicable WMDA quality standards, and each year the FGM registry assesses their compliance.

- **Maternity wards associated with a cord blood bank** (collaboration agreement**:** Act n°2011-814 dated 7 July 2011 regulates the conditions of the collection of umbilical cord blood cells and blood for potential donation and confers on them the same legal status as the other hematopoietic stem cells from the bone marrow and peripheral blood.[3])
  The maternity ward is attached to a healthcare facility and can only be associated with a cord blood bank after receiving an authorization for collection from the ARS (after the latter has received the ABM's Notice of Authorization). The list of the 16 active maternity wards participating in the RFSP is available on the ABM website.

French cord blood network (cord blood banks and affiliated maternity wards) – 2022



[3]Public Health Code Article L. 1243-5

- **The Search unit** is an EFI-accredited HLA laboratory affiliated with one or several TCs. It conducts both patient and donors HLA typing and coordinates the different stages of donor selection for a transplant, on behalf of the corresponding TC.

  Representatives of search units participate in the "WMDA search units" working group, which defines, in collaboration with transplant physicians, the procedures for querying/searching the national and international files of HSC and cord blood units donors.

- **The Transplant Center (TC):** A TC performs HSC allografts; It belongs to a healthcare facility. Healthcare facilities that offer medical education, provide medical care, and conduct medical research can be authorized to perform HSC allografts, together with healthcare facilities that have written agreements with the former in the framework of public hospital services. A five-year authorization is provided by the ARS, after it has received the ABM's Notice of Authorization The TC must comply with the quality standards of the JACIE (Joint Accreditation Committee ISTC-EBMT) — the European quality management system, under the egis of the relevant professional societies — to ensure that patients receive the best quality of care and to improve the performance of the laboratories and centers specialized in the collection, administration, and transplantation of HSCs.

  The list of authorized TCs, established from information transmitted by the ARS, is available at the ABM website. 46 facilities are authorized: 31 adult and 15 pediatric facilities.

National TCs (allogeneic) – 2022

- **The 37 international connected registries**

  The connection with the FGM registry is performed by a secured information system called EMDIS (the European Marrow Donor Information System) which gives access to all donors and cord blood units recorded in the registries worldwide.

- **The 35 international non connected registries**

  The FGM registry communicates with them directly

1.5. The scientific partners of the French stem cell donor registry

The FGM Registry works closely with professional societies, especially with:
-the French-speaking Bone Marrow and Cell Therapy Society (SFGM-TC) — FGM attends its Scientific Committee and relies on the committee of external transplant physicians experts
-the French-speaking society of histocompatibility and immunogenetics (SFHI)
-the European Blood and Marrow Transplant group (EBMT).

1.6. The WMDA

The FGM registry has been a member since 1993 of the WMDA (World Marrow Donor Association), an international association including 73 registries in 54 countries.

The WMDA issues clinical practice guidelines and establishes quality standards to facilitate international exchanges of HSCs for transplantation.

The FGM registry has been accredited by the WMDA since 2004. This accreditation guarantees that the French registry meets the WMDA's international quality standards in terms of organization, resources, and efficiency.

Information, selection, registration, and management of unrelated stem cell donors

1- Actions to promote information and awareness about stem cell donation

As part of the communication missions towards the public assigned by law to the ABM), various approaches to raising awareness of hematopoietic stem cell (HSC) donation have been implemented at the national level, in partnership with the French Blood Authority (hereafter EFS), university hospital centers (CHUs), and other organizations working to promote such donations:

- establishment of a website devoted to stem cell donation: www.dondemoelleosseuse.fr ;
- content shared by the Agency's official social networks;
- the Agency's institutional website www.agency-biomedecine.fr
- information developed and distributed by the Agency's communication division (newsletters, posters, brochures, etc;
- media relays (local, regional and national press, radio, and television);
- the annual communication campaign conducted by the Agency.

Actions to promote information and awareness about bone marrow stem cell donation are relayed at the local and regional levels by establishments and facilities called donor centers, located in the facilities of the EFS and in the CHUs, and by non-profit associations and organizations. These actions are:

- specific actions taken by donor centers;
- the organization of donor active recruitments (collaboration between DCs, associations, and the ABM);
- communication campaigns towards young people in schools and universities;
- communications campaigns in large corporations.

TCs can also participate to the promotion of the unrelated stem cell donation by informing their patients' family.

2- Registration of new donors and update of contact information

Donor registration on the FGM Registry is endorsed by the ABM. The registration costs include:

- The donor medical interview - performed onsite at donor centers or during blood collection events or:
- The management of donor registration kit shipping and returns
- The donor HLA typing
- The administrative costs.

The EFS and CHU donor centers manage these volunteers in accordance with the standard agreement signed between the ABM and the donor centers.

2.1 Pre-registration process

Preregistration is done online on www.dondemoelleosseuse.fr .

Requests for pre-registration, once validated, are transferred, via SYRENAD -FGM registry's donor management software- to the waiting list of the local DC corresponding to the donor's living address. The DC is responsible for the quick treatment of the request.

2.2 Registration processes

Various ways of registration are possible, depending on how the preregistration request was received:

- From online preregistrations via SYRENAD.
  Depending on the donor's choice:
  - A registration kit is sent to donor's living address
  - An appointment for medical interview is fixed at an EFS or CHU donor center close to the donor's living address.
- From active recruitment events.
  Volunteers come and take an appointment for a registration on a specific date at a designated place. They are informed about bone marrow stem cell donation, their pre-registration is submitted directly on www.dondemoelleosseuse.fr, and a biological sample is collected for HLA typing.

2.3 Registration

2.3.1 Information on bone marrow donation

Before getting registered, potential volunteer donors must be perfectly informed about specific aspects of stem cell donation, of the practical details of their registration and registration follow up.

This information is provided by:

- Donor Center's trained healthcare professionals. Each year, the FGM registry ensures that training is provided by donor center experienced supervisors. Alternatively, the FGM registry offers training sessions several times a year. Training must be renewed at least every 3 years (see donor centers WMDA accreditation compliance file).

The bone marrow donation official website www.dondemoelleosseuse.fr,

- Documents distributed by the ABM, which is responsible for communication on stem cell donation toward the public at the national level

The fundamental information provided to volunteer donors includes:

- The reminder of the 3 major rules of donation: Bone marrow donation is voluntary, anonymous and free of charge. (Bioethics Act);
- The vital interest of a stem cell transplant for the patients;
- The process of donation medical care;
- The different ways of collecting bone marrow stem cells, as well as their potential side effects (Ref the information booklet on the bone marrow and peripheral blood stem cell donations, as well as the initial and final donor consent form);
- The right to withdraw consent, which can be expressed at any time;
- The administrative and financial support associated with the collection of stem cells, in accordance with the current regulations for all donors;

- The importance of donor long-term commitment and to communicate any changes of address, contact information, and civil status, in order to be reachable rapidly in case donor is requested for a patient;
- The conservation of donors' biological material, which may be used for a scientific purpose, in relation with donor potential donation;
- The performance of biological tests aimed at typing donors' HLA, establishing their fitness to donate, and letting them know the results of their assessment;
- The obligation to express consent before High Court for the collection of bone marrow or peripheral stem cells (Bioethics Act) . The Judge verifies that the physician provided the necessary information during the donor mandatory physical exam, that no pressure was exerted on the donor, and informs the donor of his right to withdraw at any time.

At registration, donors sign the form called ‘’initial consent to bone marrow cell donation", which sums up the key points they must know and accept.

In view of the rule of anonymity, donors agree that they will not try to discover the identity and contact information of their recipient .(Bioethics Act).

The donor's identity is verified from an official identity document:

- presented by the volunteer at the time of the medical interview carried out on site,

or

- sent electronically by the volunteer to the donor center when registering on line.

Anyone who wishes to register on the French donor registry must automatically consent to both bone marrow stem cell and peripheral stem cell donation.

There are specific exemptions to marrow donation (see medical questionnaire for registration or continuation on the FGM registry, available via SYRENAD) where donors will be registered for a peripheral stem cell (PBSC) donation only, and this information will be noted in the file.

There are also specific exemptions to peripheral blood stem cell donation, where donors will be registered for a bone marrow stem cell donation only and this information will be noted in the file (SYRENAD).

Donors themselves cannot choose the method of donation. Only a medical contraindication to one of the two ways can lead to an exemption.

2.3.2 Selection of potential volunteers for stem cell donation

- **Age criteria**

To be included in the national registry, potential volunteers donors must be between the ages of 18 and 35 years.

Once registered, they remain on the registry until their 61st birthday. On the date of their 61st birthday, the SYRENAD application automatically and permanently deletes all of their characteristics from the database, informs the donor center concerned of the cancellation, and sends an email thanking these donors.

NB: the data of “cancelled donors” are completely deleted from the database, with the exception of those of donors who have already donated stem cells and who may be requested again for subsequent donation for the same patient. Their data are kept 30 years post donation.

- **Medical assessment at registration**

A medical questionnaire is completed before registration for all volunteer donors, regardless of how they were registered, so that their request for registration can be validated or rejected.

These volunteers must be in perfect physical and psychological health at this stage.

There are 3 questionnaires issued by the FGM Registry . These documents cannot in any case be modified without prior consent of the Registry:

- the health history questionnaire at donor’s registration, completed onsite by the physician responsible for the volunteer donor's medical interview;
- the self-evaluation questionnaire completed by the donor for online registration;
- the self-evaluation questionnaire specific to donors active onsite recruitments.

When a permanent contraindication is shown at this stage, the volunteer must not be registered. However, a volunteer with a temporary contraindication can be registered, provided that this contraindication is cleared in the weeks, even months before the HSC donation.

The 3 above mentioned documents are made available to donor centers on SYRENAD.

Substantial changes of these documents may be proposed by the HSC collection and transplant division (DPG-HSC). They will be reviewed by **scientific societies** when appropriate, and then approved by the ABM’s medical and scientific council (CMS) and, when necessary, by the ABM’s Advisory Board (for ethical issues)

The health history questionnaire at donor’s registration and the self-evaluation questionnaire must be kept in each donor's file. The files of volunteers who cannot be registered are destroyed.

- **Laboratory tests**
  - **HLA typing**

HLA typing is the only laboratory test required for registration.

HLA typing is routinely performed by an EFI accredited histocompatibility lab associated with the DC.

It enables the donor's actual registration and makes it possible for the national registry to launch a search for compatibility with patients for whom an unrelated HSC allograft is indicated.

As part of its national strategy, the Agency defines the HLA antigens to be typed and their level of resolution. This strategy can affect the typing techniques used. Since 2008, all donor typings at

registration must be performed at high-resolution or at allelic level (DNA based typing). More specifically since 2019 HLA typings have been performed by NGS (Next Generation Sequencing)

The list of alleles that may be tested is available in SYRENAD.

DNA preservation is recommended to enable further HLA typing (extended or verification).

○ Other laboratory tests

Infectious disease markers (such as CMV) and the ABO-Rh blood group are not mandatory at this stage.

Nonetheless, when the donor is a blood donor, it is strongly recommended to obtain those results from the donor's local blood bank (EFS) and add them in SYRENAD donor's file.

2.3.3 Donor registration on the national registry

The registration of potential donors is solely and exclusively done on the FGM Registry.

Thus, once donor is medically cleared and expected biological results received, the DC enters all of the information into the FGM registry database:

- Either via SYRENAD, the dedicated database management software, provided by the FGM registry;

or

- Via Electronic Data Interchange (EDI) system between the DC and FGM softwares.

Access to the SYRENAD software is exclusively reserved to the staff at DCs who have a right of access, that is, a user name (identifier) and password provided in advance by the ABM.

The following data are required:

- All available contact information (postal and email addresses, telephone numbers, additional contacts (family and friends), to ensure the donor's traceability;
- The biological data:
  - HLA-A, B, C, DRB1, DQB1 and DPB1 types;
  - the ABO/Rh blood group, if known;
  - Viral markers, if available;
- Immunologic-hematologic history:
  - Number of pregnancies;
  - Number of blood transfusions;
- Sex, weight and height, to calculate the body mass index (BMI).

SYRENAD automatically attributes to each registered donor a local anonymous identification code for the exclusive use of the donor center and a unique identifier (GRID) intended for national and international exchanges.

Donors keep these identifiers for the entire duration of their registration.

Every donor's registration file includes 3 documents: the initial consent form, signed and dated, the completed health history questionnaire, and the results of the HLA typing, validated and transmitted by the HLA laboratory. The DC inserts these documents in the SYRENAD donor tree, which is simultaneously accessible to both the DC and FGM.

3- Contacts and updating contact information for registered donors

3.1 Contacts: Mailings and e-newsletters

Every donor receives the national liaison bulletin, sent annually by the ABM's head of the communication department to all registered donors:

- Either by email;
- Or by postal mail, for donors without an email address.

The aim of this national liaison bulletin is to:

- Federate all donors around their registration procedure;
- Remind each donor of the commitment they made at their registration in the FGM registry, especially those who have not yet been invited for further tests;
- Transmit statistical information to them about the activity of the FGM registry;
- Inform them about changes in the collection and transplantation of hematopoietic stem cells;
- Remind each donor of the importance of reporting changes in their contact information or civil status;
- Remind them of the importance of reporting any information likely to result in a temporary or permanent contraindication to their donation;
- Offer answers to important or recurrent questions and collect suggestions for improvement.

3.2 Updating donor contact details

The report of any changes by donors in their contact information or civil status leads to an update of their file in SYRENAD software.

This update is made under the supervision of either the donor center or the FGM registry donor office, as appropriate.

3.2.1 Methods

Contact information is updated, either:

- by donors themselves in the registered donor section of the website www.dondemoelleosseuse.fr;
- by the donor center where the donor is registered, in SYRENAD;
- by the FGM registry donor office of the Agency directly in SYRENAD.

3.2.2 When donors move to a different residence

- **Donors moving to another national donor center**

After the donor has moved and his/her contact information has been updated:

- the initial donor center transfers the file via SYRENAD to the new donor center in France;

- The new DC validates the transfer request in SYRENAD.

Donors keep their initial local identification code.

- **When donors move abroad**

When a donor moves abroad, the DC in France systematically enters the donor's new address and complete contact information abroad in SYRENAD.

If the donor is asked for further testing for a particular patient:

- If there is a registry in the country where the donor currently resides, and if the donor agrees, the file is transferred to this registry, for it to manage the request for extended testing;
- If a transfer cannot be envisioned and the request is for blood samples, they can be:
    - collected at the donor's new place of residence and sent to the national donor center for analyses and results;
    - collected and analyzed (after a preliminary agreement) in the country where the donor is living. The results are then sent to the national donor center;

In both cases, the national donor center enters the results in SYRENAD.

If the donor is selected for an HSC donation for a specific patient, the national donor center contacts him/her to arrange:

- Either the transfer of the file to the local registry (if one exists) for local management and arranging collection,
- Or the donor's return to France for the collection period.

- **Temporary moves (less than 2 years)**

The file remains with the DC.

If the donor is asked to undergo further tests:

- The samples can be collected and analyzed in the donor's temporary country of residence. The results are then sent to the national DC;
- Blood samples can also be taken locally and sent to the national DC for analysis and reporting.

In both cases, the national DC enters the results in SYRENAD.

Donors outside France selected for an HSC donation for a specific patient are contacted by the national DC to arrange:

- Either the transfer of the file to the local registry (if it exists) for local management and arrangement of the collection;
- Or the donor's return to France for the collection period.

- **Permanent moves**

The national DC can transfer the donor file to the DC of donor' host country which has a stem cell donor registry.

If the country has no registry, the donor's file remains stored locally. The donor remains active in the local database and is managed the same way as someone moving abroad temporarily.

- **An international donor moving to France**

Only donors meeting the national retention criteria (in accordance with the medical contra-indications and the age limit criteria) can be transferred to the French registry

In case criteria are not met and the donor is requested for additional exams, the request can exceptionally be managed in France.

Requests made individually by international donors themselves will be treated as new requests for registration in the national registry.

4- Management of requests for further testing

Requests for further testing received by donor centers can concern: supplementary or confirmatory HLA typing, serologic tests to screen for infectious disease markers, or requests for blood samples.

At this stage, the donor center provides donors with all the necessary explanations of the biological tests that will be performed and responds completely to all of their questions, including about the administrative and financial management related to collection of bone marrow stem cells, in accordance with the regulations applicable for all donors (Public Health Code).

The donor center ensures that the donor has no temporary or permanent medical contraindication to HSC collection and enables completion of the medical questionnaire to remain on the FGM national registry. Once completed, this questionnaire must be inserted into the SYRENAD donor tree.

4.1 Request for additional HLA typing

DCs are responsible for:

- Contacting the donor;
- Verifying that they remain committed to the donation
- Verifying that the donor has no temporary or permanent medical contraindication to HSC collection. This verification is carried out by a physician - preferably by phone to avoid unnecessary travel to the donor- who completes the dedicated donor's retention health history questionnaire
- Performing the examination requested.

Should the DC not have any cryopreserved DNA samples from this donor, it will follow the same procedure as for blood sample requests: see 4.2).
HLA typing is performed by an EFI accredited histocompatibility laboratory associated with the DC.

The result of the further HLA typing must be at the resolution requested by the transplant center (HLA A, B, C, DRB1, and DQB1, at allelic resolution). If high-resolution typing is requested, the result must be entered without ambiguity. Otherwise, the examination cannot be invoiced.

The HLA typing requested must be performed within 14 days[4] after the DC receives this request, in accordance with the WMDA standards.

For any HLA typing cancellation request, while HLA typing is being processed, the CD has 3 weeks to submit results in SYRENAD. Beyond this period, typing cannot be submitted nor invoiced anymore.

[4] WMDA Key Performance Indicators for Registries; 10052022-WGQR-KPI 2021

4.2 Request for blood samples shipment

When donors must travel to provide a blood sample for additional HLA typing, infectious disease markers, ABO/RH blood group, or shipment to the requesting TC, the DC suggest a medical exam.

During this exam, the DC:

- Has a dedicated staff member verify the donor's identity (photo identification document requested);
- Ensures-during a mandatory medical interview- that the donor still has no contraindications to HSC donation
- Fills in the donor's retention health history questionnaire ;
- Calculates donor's BMI (donor is contraindicated if BMI>=35);
- Subsequently updates the donor's file (recent travel, pregnancies, weight, transfusions, etc.);

In absence of contra-indications:

- Collects the requested quantity and types of blood samples-requested by the TC
- Requests its local COFRAQ-accredited biological laboratory to test the following infectious disease markers required at this stage of the search, as per the national regulations:
    - HBs antigen
    - Antibody Anti HBc
    - Syphilis serology
    - Antibody Anti-HIV1-V2
    - Antibody Anti-HTLV1-V2
    - Antibody Anti-HCV
    - Antibody Anti-CMV (if negative or unknown)
- determines the donor's blood type and Rh status, if they are not known.

Should the donor's retention health history questionnaire present a potential medical issue, the donor must undergo a consultation with a physician referring to the DC, and the blood samples must not be taken/sent.

The blood samples taken must be labelled so as to preserve the donor's anonymity. The tubes must contain the donor's unique identity code (GRID) and the collection date.

The samples must be packaged in a secure box furnished by the ABM and meeting IATA (International Air Transport Association) requirements[5].
They must be transported to the address indicated by the TC, by the ABM's contractual shipping company.

The blood samples must be sent within 14 days[6] after reception of the TC's request, in accordance with WMDA standards.

The DC then enters the blood samples' shipping date and estimated arrival date in SYRENAD/EMDIS.

For international TCs not connected with EMDIS, the results are communicated through the intermediary of the FGM registry by e-mail to the DC, which enters them in SYRENAD to update the donor's file.

[5] http://www.iata.org/whatwedo/cargo/dgr/Pages/index.aspx

[6] WMDA Key Performance Indicators for Registries; 10052022-WGQR-KPI 2021

The DC must imperatively inform potential donors if they are selected for the potential recipient or released, should there is an HLA match or not.
When no result has been transmitted by the TC within 6 weeks after the blood samples were sent, the FGM coordination team will contact the TC to enquire about the situation so that the donor can be informed.

The transplant center's HLA typing results are entered in SYRENAD by this center if it is a national transplant center. The results are sent via EMDIS if it is an international transplant center. In case the HLA level of typing sent via EMDIS is more extended than the one currently recorded in Syrenad, then the donor center must accept this new HLA, except in particular cases.

If the DCs are unable to contact the donor after many attempts, they must immediately inform the donor department of the FGM registry, which will trigger an active search via its dedicated service provider responsible for looking for donors who no longer resides at the address given.

5- Management of a national unrelated donor selected for a national or international patient

5.1 Management of a national donor contacted for an HSC donation (First donation and subsequent donations)

- The final selection of donors by national transplant physicians or international registries is addressed to the donor center through the FGM registry.

- In France, donors have already agreed to any type of stem cell collection, unless one type is medically contraindicated for the donor. In that case, the transplant center is informed and decides whether or not to continue with this donor.

5.1.1 Information and management of donors selected for an HSC donation

The donor center must:

Contact the volunteer donors to inform them of their final selection for a patient and to offer them an appointment with a physician;
Specify to the donor the type of HSC that the clinician wishes to obtain for the patient (bone marrow or peripheral stem cells).

Ensure that the identity of the donor has been verified by a specific staff person each time that the donor appears onsite for appointments (photo identification required) especially on the final consent form and on the Health history questionnaire for use at time of work up (CF/CI051) “Health history questionnaire for use at time of work up”;

Inform the volunteer donor as clearly, objectively and precisely as possible about the entire collection procedure, its advantages and disadvantages as well as its potential side effects, simultaneously orally and via an information letter given to them about either the bone marrow stem cell donation or the peripheral stem cell donation, depending on what is being proposed to the donor (see the two information letters of the ABM and the SFGM TC donor information booklet);

Review with the volunteer the main rules of donation (see 2.3.1);

Check that donor’s commitment is genuine;

Ensure that donor is fully cleared for donation;

Provide the donor with a detailed informational document, published by the Agency, that reviews the main stages of donation of bone marrow or of peripheral blood stem cells (PBSCs);

Inform the donor of the possibility of being requested for a second donation (=around 10% of donors in the 2 years following the first donation) for the same recipient. The transplant physician must be immediately notified if donors state at this stage that they do not want to make a second donation;

Indicate to the donor the exact location of the collection and the chronology of its different stages;

Verify that the donor and CC accept the collection dates requested by the transplant physician. If not, two alternative dates must be proposed;

Communicate the detailed schedule of these arrangements to the donor;

Communicate the final schedule to the FGM registry as early as possible;

Answer all questions the donor might have about the donation and its arrangements so that the donor can provide informed consent (required for all donations except for donor lymphocyte infusion) at the local High Court in accordance with the applicable regulations.[7]
Donors are informed that they can withdraw their consent at any time; Meanwhile they are also informed about the stakes for the patient, especially during the period of pretransplant conditioning;

Provide the donor with a an emergency medical telephone number that can be used at any time, 24/7 during the immediate pre- and post-collection period;

Inform the donor that their biological samples might be kept, in association with the donation made for the patient.

Inform the donor that, in the event of a health issue occurring after the donation, he must inform the donor center, which will quickly forward the information to the FGM registry. FGM will be responsible for informing the TC, if this health issue can affect the health of the transplanted patient.

Once firmly recruited, donors must remain reachable, avoid situations at risk of infection (e.g., tattooing, piercing, endoscopy, dental surgery, multi-partners sex, etc…) and provide the donor center with contact information in case of travel.

5.1.2 General organization for HSC collection

The donor center, working with the CC, manages the general organization of the collection:

- Medical appointments (anesthesiologist, hematologist, cytapheresis specialist, other physician specialists, when necessary);
- Clinical, paraclinical, and laboratory assessment of donor clearance;
- Appointment with the CC to fix the collection date;
- Appointment with the cell therapy unit (CTU) to manage the product collected;
- Verification of the arrangements for the transport of the graft to the transplant center;
- Verification that the CTU has requested authorization to export the cells collected, if they must be transported to another country;
- Positioning of the labels provided by the FGM registry on the HSC transportation container.

At the request of the transplant center, a blood sample from the donor may be shipped in the month preceding the donation, for supplementary local tests.

In case TC plan to have the donor participate in a protocol, whose main objective concerns the conditions of the donation or involves an experimental treatment of the cells collected from the donor, intended to patient's infusion, TC must provide the FGM registry with the following documents:

- A summary in French and/or English of the protocol;
- An informational document in French for the donor;

[7] Articles L. 1241-1 and R. 1241-4 et seq of the Public Health Code

- An anonymous consent form for the donor, which will be signed by both the donor and the physician at the donor center responsible for informing the donor.

The original version of the consent form will be stored at the CC; a copy will be sent to the donor center, the cell therapy laboratory, and FGM.

On receipt of the signed consent form, FGM will send an attestation of the donor's consent to the transplant center.

The volume of the blood sample requested must be included in the assessment of the entire blood volume collected as part of the predonation work-up.

Clinical trial protocols for allogenic grafts in which the graft is used as a source of HSC, including after cell sorting or treatment by an authorized method as part of transplant not involving experimental treatment of the cells collected are considered to be a medically validated use of HST donation and therefore do not require specific consent by the donor.

5.1.3 Specificities associated with stem cell donation

The age limit for bone marrow donation is set at the donor's 61st birthday.

The collection can be performed either by traditional hospitalization or on an outpatient basis (see deliberation n°2013-16 of the Medical and Scientific Committee of the Agency, dated June 18, 2013).

The donor center ensures that all of the following appointment are made:

- Mandatory consultation with an anesthesiologist;
- Appointment at the operating suite, traditional or on an outpatient basis;
- Reservation of a bed in the case of standard hospitalization, in the medical department, and if possible in a single room;
- Appointment with the physician collecting the stem cells.

The hematologist prescribes oral iron supplementation for the donor, after verification of laboratory results including measurement of blood ferritin levels (deliberation n°2015-12 of Medical and Scientific Council of the Agency, dated June 16, 2015).

The physician collecting the cells validates the prescription for bone marrow stem cells by the transplant physician or indicates the maximum quantity forecast of total nucleated cells (TNC) from the bone marrow likely to be collected from the donor.

Below we report the calculation used to make this estimate (see studies from the NMDP registry and the FGM registry):

Theoretical method of calculation:

Donor weight in kg x 20 mL

= maximum volume to collect x 0.18

= theoretical quantity of TNC to collect

5.1.4 Specificities associated with PBSC donation

The age limit for a PBSC donation is the same as for a bone marrow stem cell donation --- the donor's 61st birthday (see ANSM decision dated February 7, 2020, defining the good practice rules about the collection of human body tissue and cells from a living or deceased person, for therapeutic use).

The donor center is responsible for making the appointment for PBSC collection at the cytapheresis center.

At the predonation examination, a qualified and authorized physician prescribes:

- Hematopoietic growth factors at 10 µg/kg/day, in 2 daily subcutaneous injections of 5 µg/kg each, for 4 to 6 days,
- Their injection by a registered nurse, at the donor's home if necessary,
- Minor analgesics, for the donor to use in case of pain.

The donor will receive a document for monitoring the injections to be performed and their effects.

The prescribed product must be supplied by the central hospital pharmacy.

The hematologist who prescribes G-CSF ensures that hyperleukocytosis greater than 70,000 is detected and managed in accordance with the recommendations of the high authority for health (HAS).

If the total number of white cells exceeds 70 000/mm3, it is recommended that the G-CSF injections be stopped until the first cytapheresis.

Donors must be informed that they might have to donate bone marrow on an emergency basis (in the 24-48 h after the last cytapheresis) if the PBSC collection procedure fails.

Once the hematologist of the DC has seen the results of all of the biological and paraclinical tests (see opinion of the Medical and Scientific Council of the Agency, dated June 16, 2015) and has verified the quality of the donor's venous access, he/she validates the donor's clearance.

The DC gives the donor a sheet for monitoring the G-CSF injections to complete and give to the physician collecting cells at the first cytapheresis (verification of the actual performance of the injections, of the nature and intensity of the side effects associated with the injections of the product).

The DC must manage arrangements for the immediate pre- and post-donation medical monitoring, in particular by giving the donor the telephone number of a physician reachable 24/7 who is a member of the medical team to which the G-CSF prescriber belongs.

The DC provides the donor's complete predonation file, including the hematologist's validation, to the physician performing the cytapheresis.

The cytapheresis physician validates the feasibility of the PBSC request formulated by the transplant physician. The quantity of CD34+ cells and the presumed number of cytaphereses (maximum: 2) are communicated to the transplant physician through the FGM registry, before the patient's conditioning begins.

A single cytapheresis must be preferred. If a second session of cytapheresis appears necessary (because large quantities of CD34 cells are expected), it is recommended to organize the first session, if possible, on the afternoon of the first day, and the second session on the morning of the second day, to reduce the storage time of the first sample and facilitate the transport of the entire graft to the transplant center.

When the donor's home is far from the CC, a hotel room can be reserved for the day before the first collection or between the first and second collections, if a second is scheduled. The accommodation costs due to the donation are covered.

If the donor's medical situation so requires, the costs of an accompanying person can be covered (see Guides for the financial coverage of living donors of materials from the human body/ Agence de la biomedicine)

In no case should donors be hospitalized between the 2 cytaphereses, unless their clinical status so requires.

5.1.5 Specificities associated with donation of mononucleated cells/lymphocytes

The age limit for the donation of mononucleated cells (MNC) is reached the day before the donor's 61st birthday. (see ANSM decision dated February 7, 2020, defining the good practice rules about the collection of human body tissue and cells from a living or deceased person, for therapeutic use).

This type of donation takes place without G-CSF stimulation.

A physical examination remains mandatory for the donor, but need not be performed by a hematologist.

The confirmation of the donor clearance is sent by the physician at the donor center who performed this examination.

The donor's consent to donation by cytapheresis must be collected locally, but the law does not require that it take place before the High Court.

If the venous approach is difficult, a whole blood sample can be envisioned, with the agreement of the transplant center.

The physician performing the collection must validate the prescription of mononucleated/CD3 cells and define the methods for cytapheresis, based on the quantity of cells requested and on the donor's characteristics.

A single session of cytapheresis will be performed. If needed, another session may be scheduled later on, if the donor's blood count allows it.

5.2 Final validation of medical fitness to donate HSCs

The final donor clearance assessment must take place in the **30 days** before the HSC/MNC collection.

The Physician determining donor clearance must reject any donors with a contraindication to donation which would jeopardize their own safety. This information is transmitted to the FGM registry via the donor center (see form CI014 “Donor final clearance”).

If the contraindication threatens the recipient's safety, the transplant physician is informed and the final decision about continuing or not with this donor is taken together with the physician who saw the donor, FGM, and the transplant physician (see form CI070 “Notification of critical information”).

The reasons for stopping the procedure must be explained to donors by the physician who saw them.

The physician determining the donor final clearance must not be the transplant physician taking care of the patient, to avoid any conflict of interest[8].

The donor center assembles the entire file which includes:

The report of the hematology, anesthesia, and cytapheresis consultations, as well as any other consultations when applicable;

The minimal laboratory and paraclinical results (see, Referral to the Medical and Scientific Committee of the Agency, dated June 16, 2015):

- blood count, platelets
- CBC platelets, PT, ACT, fibrinogen
- Blood electrolyte analysis: urea, creatinine, Na, K, Cl, Ca, Mg
- glycosylated hemoglobin
- Liver function tests: ASAT, ALAT, total bilirubin, alkaline phosphatases, gamma GT
- Ferritinemia, coefficient of transferrin saturation
- Electrophoresis of serum proteins (for donors over 50 years old)
- ABO group, Rhesus and Kell phenotypes (testing should be planned before the donation)
- Irregular antibody screening
- Anti-alpha and anti-beta hemolysins, when pertinent;
- Serum pregnancy test. If it took place more than 7 days before the planned collection date, it must be repeated just before patient conditioning begins, or before G-CSF injections begins if the patient conditioning is less than 5 days (see JACIE standards).
  The donor must be reminded to avoid becoming pregnant throughout the period preceding the stem cell collection. The form CF/CI051 “Health history questionnaire for use at time of work up” requires the mention that this information was provided to the donor.
- Electrocardiogram in case of clinical warning sign
- Cardiology consultation and echocardiography (for donors over 50 years old);
- Face/profile chest X-ray (for donors over 50 years old).

Depending on applicable health safety rules, the clinical screening of the volunteer donor must be completed by laboratory tests intended to diagnose some transmissible infectious diseases.

[8] WMDA Standards (version 2020) 3.22.3.1

A decree of the Minister of Health lists the infectious diseases that must be screened for systematically[9].

The list specifies:

- HBs Ag;
- Anti-HBc antibodies;
- Anti-HBs antibodies (if HBc Ab-positive);
- HBV DNA;
- Anti-HCV antibodies;
- HCV RNA;
- HIV 1+2 antibodies and p24 Ag in a combined test;
- HIV RNA;
- Anti-HTLV 1+2 antibodies;
- Syphilis serology;
- Anti-CMV antibodies (IgG or IgG + IgM);
- Ant-EBV antibodies (IgG anti VCA or IgG anti EBV);
- Anti-toxoplasmosis antibodies (IgG or IgG + IgM);

This minimal assessment can be extended, depending on the conclusions of the medical visit and the donor's potential past exposure to specific infectious agents by extended testing:

- Situation at risk of infection onset in the 4 months before the HSC collection: additional PCR of the HIV, HBV, and HCV markers to be performed before the patient begins conditioning. The result must be available at least 24 h before the conditioning is planned to start.
- Chagas disease, West Nile virus, malaria, chikungunya, Zika, and dengue, SARS-CoV-2, TBEV… or any other infectious disease marker, in accordance with the guidelines issued by the HCSP and after a stay in areas at risk of infection, or upon international registry request.

Special cases:

- Hepatitis B positive markers:
  HBc Ab-positive, HBs Ab-positive, and HBV-DNA negative-> HSC graft possible;
- Hepatitis C-positive markers:
  HCV Ab-positive and HCV RNA-negative -> HSC transplant possible.

Validation of the donor clearance or non-clearance, including all of the results of the tests performed and verification of the donor's identity (see form FGM CF/CI014 ‘’Donor final clearance’’) must be transmitted, before the start of the patient's conditioning, to the FGM registry, which forwards it to the TC.

Upon donor request, these test results are transmitted to them and/or their general practitioner. The physician supervising the donor center informs the donor directly of any clinical, paraclinical, or laboratory anomalies or if any infectious disease marker is positive.

The results are valid for 30 days from the date of sample collection.

If the collection is delayed beyond 30 days from the date of sample collection, the whole assessment must be repeated (ANSM decision of February 7, 2020 defining the rules of good practice relating to the sampling of tissues and cells from the human body on a living or deceased person, with a view to therapeutic use) and it includes : the infectious and biological assessment,

[9] Decree of June 22, 2011 on the procedures for performing medical biology analyses for the detection of infectious markers on elements and products of the human body taken for therapeutic purposes, with the exception of gametes, blood and blood products, supplemented by the ANSM 2013 Recommendations

as well as the health history questionnaire and the travel history which must be updated after a medical consultation (hematologist), or a teleconsultation. Documents relating to donor final clearance that have been updated must be dated and signed.

5.3 Information and consent of a national donor [10]

"The collection of parts of the human body and of its products cannot be practiced without the donor's prior consent. This consent is revocable at any time." Article L. 1211-2 of the Public Health Code

During recruitment of donors in France for a first bone marrow stem cell or peripheral stem cell donation, the physician responsible for the final fitness validation must provide them with specific and exhaustive information related to the donation process and the risks associated with it (see Information note and final commitment of the unrelated donor of HSCs from the bone marrow or peripheral blood).

Donors then sign the final consent form, attesting that they have received all of the information necessary before agreeing to the donation.

Donors take this duly signed document with them and go to the High Court of their residence-or of the place where the collection will take place- to formally obtain the consent by High Court Judge who checks their identity and ensure that their consent is voluntary and informed. (see, Bioethics Act dated 7 August, 2004, and the Public Health Code).

The principle is to be certain that the donor has received complete and exhaustive information:

- About all of the procedures associated with the arrangements for the collection;
- The potential risks;
- And the revocable nature of the consent.

The DC sends to the FGM registry a copy of the signed donor's written consent obtained from the High Court and also ensures that donor received a copy.

In some cases, collection may have to be delayed for several weeks to several months for various medical reasons. In those cases, the ABM recommends that the DC has the donor sign the final consent form again, but not require him to return to the High Court if the delay has been less than one year.

Moreover, donors must be informed that they can be requested for a second donation to the same patient, within a variable time limit. In case of donor withdraw, FGM inform the TC immediately.

5.4 Archiving the donor's file

The donor's complete file must be archived in conditions guaranteeing its safety and confidentiality for a period of 30 years, simultaneously by the donor center and the FGM registry, regardless of the medium — paper or digital (Public Health Code - article R1112-7 and Rules of good practices for tissue-cell collection, dated 7 February 2020 2020).

6- Collection of hematopoietic stem cells and mononucleated cells (lymphocytes)

Hematopoietic stem cells (HSCs) and mononucleated cells (MNCs) are collected in centers duly authorized by the regional health agencies (ARS).

[10] Articles R. 1241-3 and R. 1241-4 of the Public Health Code

They are the object of a written procedure, specific to each type of collection; the procedure includes the labelling and traceability of the products, in accordance with the rules of good practices for tissue-cell collection, dated 7 February 2020, and the relevant regulations in force (Decree no 2007-519 dated 5 April 2007, relative to the conditions of the authorization of cell collection and modifying the Public Health Code (regulatory provisions).

CCs must ensure the protection and confidentiality of the donors' personal data, of which they are custodians, though the referring donor center. (see JACIE accreditation, version 8 - March 2021).

Collection is arranged under the supervision of a qualified, experienced health professional (see JACIE version 8 - March 2021 and EFS framework documents/national procedures, September 2018: training and authorization of physicians and nurses at EFS health centers).

Once a donation is completed, donors are removed from the national database of active donors and can no longer be solicited for another patient.

They remain on the list of donors cancelled because their donation was completed, so that their contact information can be updated and a second donation can be requested for the patient who received the first one.

The age limit for bone marrow donation is set at 60 completed years (61st birthday).

6.1 Bone marrow collection

The healthcare facilities authorized to perform HSC allografts are also authorized to collect bone marrow stem cells; some can also collect peripheral stem cells.

6.1.1 Donor hospitalization

The procedure can involve either:

- Traditional hospitalization, that is, admission the day before the procedure and discharge the next day,

or

- outpatient hospitalization, according to the procedures in force .

6.1.2 Stem cell collection

Bone marrow is collected in a sterile operating room. Under strict aseptic conditions, the patient is placed in a ventral decubitus position, under general anesthesia, and the bone marrow is collected from the posterior iliac crests.

Collection from the anterior iliac crests is not recommended and can be considered only if the donor was warned about this possibility in advance and agreed.

An intermediate count of total nucleated cells (TNC) during the collection is recommended to ensure that a sufficient number are collected in the minimum possible total volume.

On request, blood samples can be collected during bone marrow donation, for the performance of further tests. They will be transmitted together with the bags containing the graft.

Even when not specifically requested, the routine inclusion of 5 mL of the donor's blood is recommended; it should be collected into a dry tube for potential retrospective studies of infection (blood sample on D0 of the HSC collection) and to check the ABO/Rh blood group.

The bone marrow is collected with the anticoagulant and placed in the medium specified by the transplant center.

The bone marrow collected is packaged in appropriate bags, in accordance with the written protocol and in accordance with good collection practices (maximum sample = 20 mL/kg donor weight).

The collection report includes all the information necessary for the characterization of the cells collected, for the patient considered.
FGM form CI023 “Bone Marrow Collection/Delivery Report” or the form specific for the international CC, must travel with the graft, and must also be sent by email to the FGM registry.
The form must specify whether or not the bone marrow has been filtered.

6.2 Collection of peripheral stem cells

6.2.1 G-CSF injection

If possible, the G-CSF must be provided to the donor by the hospital's central pharmacy, on the prescription of the hematologist who examined the donor suitability to donate; payment for the G-CSF for the donor is included in the annual transplant package (FAG) paid to the TC.

The physician prescribing G-CSF ensures that hyperleukocytosis greater than 70,000 is detected and managed in accordance with the recommendations of the high authority for health (HAS).

If sufficient CD34+ cells are circulating, the CC must consider advancing the collection date and informing the FGM registry, which is responsible for transmitting this information to the transplant center or international registry concerned, as necessary.

Donors receive a questionnaire on which they assess and report daily the immediate side effects of the growth factor injections (form available on SYRENAD).
This completed questionnaire also makes it possible to verify the regularity of the subcutaneous G-CSF injections.

From 24 hours before the G-CSF injections begin and through the entire period of injections, collection, and for 24 hours after the donation, the donor must have available a medical telephone number that is accessible 24/7.
Similarly, donors must be reachable at all times by the donor center, to be able to warn the donor if the procedure is being stopped.

It is specified to any lady donor breastfeeding her child to stop breast-feeding from the first day of injection of the GCSF, throughout the duration of the injections and one week after the last injection. She can express her milk to maintain lactation, but must neither store it nor give it to her child.

6.2.2 Organization of peripheral stem cells collection

PBSC collection takes place on D4, D5, or even D6 after G-CSF administration began, and must not exceed 2 cytapheresis.

The positioning and surveillance of the donor, as well as the duration of the cytapheresis procedure, follow the orders of the physician responsible for it and the regular procedures of the facility.

Placement of a central venous catheter is strictly prohibited (see Good Collection Practices rules dated 7 February 2020). If the venous condition or if the mobilization of the donor is poor, the TC will be informed by the FGM coordination and the donor will be prepared for a bone marrow donation (TC previously informed of the procedure).

On the explicit written request of the transplant physician, donor blood samples can be collected the day of the PBSC collection, for further tests. They will then be transported with the PBSC graft.

The number of cells of this product is counted on the day of collection, by the cell therapy laboratory associated with the CC.
The results are sent to the FGM registry for communication to the TC.

If the expected quantity of CD34+ cells is not reached at the end of the 1st day of apheresis, a second session is set up for the next day, provided that donor is medically cleared to continue.

Except in specific cases, the graft must not be manipulated at the collection site.
The collection report includes all the information necessary to characterize the collected product, intended to the recipient.

FGM CI023.2 form “PBSC collection/delivery report” or the form specific to the international collection, must travel with the graft, and must also be sent by email to the FGM registry.

6.3 Collection of mononucleated cells/lymphocytes

A donor who previously gave HSCs can be requested for a subsequent donation of mononucleated cells (lymphocytes).

The collection procedure (lymphapheresis) is similar to that for PBSC collection.
Nonetheless:

- This collection does not require the preliminary administration of growth factors;
- Consent at the High Court is not required;
- A single session of lymphapheresis is performed.

If needed, a second session of lymphapheresis can be performed, at least one month after the date of the first session, after the donor is fully informed and has consented.

6.4 Labelling, packaging of bag(s), and required documents

The bag(s) containing the PBSCs collected must be correctly sealed, and their labelling and packaging must comply with the ANSM decision dated 5 May, 2017, modifying the decision dated 27 October, 2010. The unique European code SEC is used by the cell therapy laboratory to ensure the identity and traceability of the product collected (the graft).

The collecting physician completes the summary collection report (see FGM CF/CI034 form “lymphocytes collection/delivery report”), attaches it to the graft collected, and ensures that it is transmitted to the FGM registry.
The bags are wrapped in protective fabric. Each bag is wrapped individually in a closed plastic package.

The blood tubes are placed in a separate package, to avoid contact between the glass and the bags, in case the tubes break.

The bags and blood tubes are placed in an insulated travel container.

The donor must remain anonymous. Only the donor anonymity code (GRID) is used.

7- Transportation of grafts of hematopoietic stem cells and mononucleated cells (lymphocytes)

7.1 Preface

The collected PBSCs for transplantation are transported by a person designated by name and appointed by the national or international transplant establishment.

It must be a person who is part of the transplant center team or working for a shipping company selected by the transplant center.

Every measure is taken to enable the graft to be transported as rapidly as possible, depending on the distance to travel and in any case, within less than 72 hours.

7.2 Transport organization/arrangements/preparation of transport

The transport is jointly organized by the national or international transplant center/the associated cell therapy laboratory, the FGM registry, the international registry for international patients, and the transport company assigned by the transplant center.

For international exchanges with other countries (outside the European community), an import/export authorization, depending on the situation, must have been obtained from the ANSM before the graft leaves and insofar as possible before the patient's conditioning begins.

The transporter must be in possession of an insulated container, made available by their establishment and equipped with temperature control equipment.

National donor centers and patients in France

The FGM registry produces a digital transport file, which is transmitted to the donor center to facilitate the graft delivery. This file comprises:

-the shipper's cover sheet, with recommendations to the courier,
-labels to print and attach to the string label,
-the itinerary validated by the transplant center (form CF019 “Courier details”)
-verification of the prescription,
-questionnaires concerning the follow-up of the donor from whom the transplant was collected,
-the PBSC/Bone marrow collection/delivery report (form CF023),
-the customs page, French version only

Moreover, the coordinating team sends to the donor center a letter thanking the donor, accompanied by a symbolic hourglass.

National donor centers and international patients

The FGM registry produces a digital transport file, which is transmitted to the donor center to facilitate the graft delivery. This file comprises:
-labels to print and to attach to the string label,
-verification of the prescription,
-the forms concerning the follow-up of the donor,
-the PBSC/Bone marrow collection/delivery report (form CI023),
-the shipper cover page, in English
-the customs page, in both French and English versions
-the export authorization delivered by the ANSM, for countries outside the EEA

Moreover, the coordinating team sends to the donor center a letter thanking the donor, accompanied by a symbolic hourglass.

8- Insurance for unrelated donors of hematopoietic stem cells

The ABM, as a public administrative establishment, is self-insured.

This insurance covers, on a subsidiary basis, unexpected events that are not already covered by the insurance of the hospital center or the EFS in respect of their prevention, diagnosis or care activities, by ONIAM in respect of national solidarity, or of the donor in respect of his civil liability.

DCs must declare any incidents occurring during medical examinations of donors at registration or at blood sample or hematopoietic stem cells collection- where applicable- to FGM, should these incidents fall under the warranty of the BAM.

Incidents are covered by the ABM warranty at the pre-donation stage, and at the post-donation stage within a limit of 10 years. In all cases, a cause-effect relationship must be established.

9- Reimbursement of expenses to hematopoietic stem cell donors

« No payments, in any form, can be made to the persons who allow the collection of components of their body. The expenses accompanying the collection are entirely covered by the healthcare facility responsible for this retrieval"
Article L. 1211-4 of the Public Health Code

The principle of free donation has the corollary of financial neutrality, which guarantees donors full reimbursement of the costs they have incurred for the donation to be made and/or the donation made.

The healthcare facilities in charge of the collection have the obligation to guarantee the financial neutrality of the donors, so that the entire donation process and the subsequent medical follow-up do not incur any expense for which they are responsible. They must therefore proceed directly to the reimbursement of all the costs incurred by the collection and its organization to the donor.

9.1 Procedures for the reimbursement of donors' expenses

The methods of reimbursement of the donors' expenses are described in the guide for the financial coverage of living donors of human body components,[11] produced by the Agency.

Donors are reimbursed by the center collecting the graft, on production of the necessary supporting documents, which concern:

- The transportation costs related to:
  - Examinations and tests before and after the collection;
  - the trip to the High Court to express consent;
- Compensation for lost salary/remuneration;
- Accommodation expenses, when applicable

A document, drawn up by the administrative and financial department of the ABM, indicating the reimbursement ceilings, is sent for information to the DCs, Collection Centers (hereafter CCs) and TCs as well as to the financial departments of the centers concerned, each time these ceilings are updated by the central administration. This document is also available on request.

11 Guide for the financial coverage of living donors of human body components - Agence de la biomedicine

9.2 Re-invoicing the TC for collection related costs

9.2.1 In the case of an HSC donation for a national patient

The DC re-invoices at cost to the TC all the costs reimbursed to the donor, in strict compliance with the anonymity of the donor (documents and invoices show the anonymity code only).

9.2.2 In the case of an HSC donation for an international patient

The CC re-invoices to the ABM - which provides financial intermediation with the corresponding international registry - all the costs reimbursed to the donor, in strict compliance with the anonymity of the donor (documents and invoices show the anonymity code only).

10- Request for subsequent donation

The DC immediately inactivate any donor who has donated HSC for a patient from SYRENAD database. Those donors therefore can no longer be requested for another patient.

They nonetheless remain "reserved" for the patient who received their first HSC donation, should that patient require a second donation, of either HSC or lymphocytes.

Indeed, over a variable period that may range from one month to several years, some donors who have already donated can be requested for a second donation for the same patient. This second donation can be either a bone marrow (hereafter BM), PBSCs, or lymphocytes donation.

There is no age limit for a second donation. However, should the donor be over 60 year old, the collection is carried out only upon issuance of a written waiver granted by the CEO of the ABM, after validation of donor clearance and consent.

Any donor who gave BM cells in a first donation can be asked for a second BM donation, or PBSCs, or lymphocytes.

Any donor who gave PBSCs in a first donation can be asked for a second donation of PBSCs, BM or lymphocytes.

The procedure for the donation request is then the same as that for the request for the first donation.

NB: a related HSC donation subsequent to an allogenic donation is possible, if donor’s health allows it and if donor represents the best choice for the family member. The TC physician must be notified of the first unrelated donation.

11- Follow-up of HSC unrelated donors

11.1 Immediate follow-up of HSC donors

11.1.1 Bone marrow donors

The CC is responsible for the follow-up of bone marrow donors from the day of stem cell collection and throughout donor’s hospitalization. A collection report is completed by the harvest physician and transmitted to the FGM registry.

A follow-up questionnaire, developed by the FGM registry and intended for donors allows them to share their comments and feelings concerning the entire donation period.

The harvest physician or another team member must visit the donor the day of the donation, to respond to the questions he/she may have.
The donor's discharge is subject to the medical authorization of the physician in charge; In case of a bone marrow collection on an outpatient basis, the anesthesiologist must countersign the discharge.

Sick-leave can be prescribed for donors[12] depending on their clinical condition and laboratory results post-donation; its duration should depend on their physical activity. The sick-leave is generally a week between the admission for bone marrow collection and return to work.

A laboratory assessment must be performed during the month after the donation to check, in particular, the hemoglobin level.

A letter must be sent to donors' general practitioner to inform him/her of the donation and the follow-up required.

The DC must contact donors by telephone in the days right after the donation to check their health status.

Donors are informed that they must alert the donor center if they have any health problems or unexplained fatigue possibly associated with this donation.

In the event of any donor pathology occurring after the donation, likely to affect the state of health of the transplanted patient, the DC will quickly communicate the information to FGM, which is responsible for informing the TC.

Two follow-up questionnaires are sent to the donor (available on SYRENAD); the first is to be completed immediately after the collection and handed to the CC, and the second must be completed 1 month after the donation and sent by mail to the DC.

Upon reception, the DC enters the follow-up information in the SYRENAD database.

11.1.2 Peripheral stem cells donors

From the day of the first G-CSF injection to the collection day PBSC donors are followed up by the team of hematologist to which the doctor prescribing the G-CSF at pre-donation stage belongs (the donor must have a telephone number that can be reached 24/24, 7/7), .Throughout the collection procedure they are followed -up by the CC team..

A collection report is completed by the collection physician and transmitted to the FGM registry.

Three follow-up questionnaires developed by the FGM registry are handed to donors at their predonation visit for completion:

the first is to be completed during the G-CSF injections (Table for follow-up created by the FGM registry and available on SYRENAD);

The second is completed immediately after the collection and handed to the physician who performed it;

The third questionnaire must be completed by the donor 1 month after the donation and sent by mail to the DC.

Upon reception, these questionnaires are analyzed and any necessary action taken. Then the DC enters the follow-up information in the SYRENAD database.

[12] Circular DSS/DH/DGS/2000 N°2000-357 dated June 30, 2000, relative to coverage of costs related to collection of organs, tissues, or cells, including gametes, from the human body for therapeutic purposes

Sick-leave can be prescribed for donors, depending on their clinical condition and laboratory results before and after the donation. Its duration should depend on the donor's physical activity and general health status. The sick-leave after collection is generally a week between the beginning of the C-CSF injections and return to work.

A biological check-up must be performed several days after the donation-most often between 3 and 10 days - to verify the platelet and total white cell count, and to identify any potential lymphopenia.

A letter must be sent to the donor's general practitioner to inform him/her of the donation and the follow-up required.

The donor center must contact donors by telephone in the days right after the donation, to check on their physical and mental health status.

Donors are informed that they must alert the donor center if they have any health problems or unexplained fatigue potentially associated with this donation.

In the event of any donor pathology occurring after the donation, likely to affect the state of health of the transplanted patient, the DC will quickly communicate the information to FGM, which is responsible for informing the TC.

11.2 Long-term follow-up of HSC donors

Donor centers must follow up unrelated HSC donors yearly for 10 years after the donation.

Moreover, donors are informed that they must alert the donor center or the FGM registry, which will direct them to the corresponding Dc, should their health condition change at any time in the 10 years after the donation.

The DC is automatically informed via SYRENAD of the anniversary date of donations (BM or PBSC) and must then contact the donors concerned, to inquire about their health and outcome since the donation.

In the event of any donor pathology occurring after the donation, likely to affect the state of health of the transplanted patient, the DC will quickly communicate the information to FGM, which is responsible for informing the TC.

This follow-up questionnaire can be completed by the DC physician during a telephone interview or be mailed to the donor. In the latter case, the donor must complete it and send it back to the DC.

This annual follow-up questionnaire is:

- Reviewed by the DC;
- Data are entered into SYRENAD by the DC in the corresponding donor file;
- Digitalized and placed in the SYRENAD donor tree. Otherwise, it must be archived locally in the donor's paper file.

The DC ensures that the donor contact details are up-to-date – should the donor be requested for subsequent donation.

12- Donor anonymity

"The donor must not know the recipient's identity, nor can the recipient know that of the donor. No information enabling the simultaneous identification of the person who donated their body components or products and of the person who received them can be divulged." Article L. 1211-5 of the Public Health Code

In compliance with the legislation in force, unrelated HSC donation is strictly anonymous.

This anonymity is extended in France to donors and recipients, in France and internationally.

Before being registered on the FGM registry, the donor undertakes to adhere to this principle of anonymity and signs the initial consent form.

12.1 Respect for donor anonymity/Exchanges of information between the DC and the Search unit

The donor's identity must never appear in any document intended for a TC.

Donors must always be mentioned by their unique anonymous identifier code (hereafter GRID).

Both donor's blood samples and HSC bag must only show donor GRID and collection date (on tubes and documents)

12.2 Correspondence between the donor and the recipient

The anonymous correspondence between the donor and the recipient is permitted.

All correspondence must be transmitted by the DC, TC, or international registry to the FGM registry, which ensures that the principle of anonymity is respected. FGM staff member will translate the mail- if necessary- and then send it to the donor or transplant center responsible of the corresponding recipient.

No exchange of gifts, regardless of the value, is allowed.

13- Conditions of cryopreservation of the hematopoietic stem cells of an unrelated donor

Cryopreservation of the entire HSC bag can be requested, with supporting arguments or upon acceptation of the TC. It can only be carried out with the written approval of the transplant physician.

The donor must be informed of this project, as per mentioned in the "final consent form" signed by the donor.

The presumed date of the transplant is specified by the transplant physician before the collection and cryopreservation of the HSC.

The cryopreservation of the entire graft must remain exceptional and requested in the following situations only:

- donor's unavailability at the dates requested by the TC, and any other acceptable dates are possible;
- unexpected patient's medical complication, which delays the planned infusion date
- any exceptional situation making the delivery of the graft uncertain.

Cryopreservation of the HSC product must be carried out by the cell therapy unit of the TC, upon immediate receipt of the harvested graft, except in duly justified exceptions (long distance, transport hazards, aso.) and after approval from the national or international register.

If the transplant project is cancelled (in the event of a change in the indication for the transplant or the death of the patient), the cryopreserved HSC product must be destroyed. In the "final consent form" signed by the donor, the information of potential non-use of the product is specified to him.

A certificate of destruction must be sent by the cell therapy laboratory to FGM for information.

Registration and management of unrelated cord blood units

1- Mothers' information and awareness about cord blood donation

As part of its responsibilities for communication with the general public, the *ABM* has taken various steps to raise awareness about the donation of cord blood at the national level:

- Establishment of a website devoted to cord blood donation: www.dondesangplacentaire.fr;
- The creation and distribution of brochures intended for all the healthcare professionals concerned working in our partner maternity units and for the pregnant women interested by this donation.

Pregnant women who might be interested in donating cord blood and are giving birth in one of the maternity affiliated with a cord blood bank (that is, a member of the French cord blood network (hereafter RFSP) receive complete information during their pregnancy, provided by staff who are qualified and trained to provide it.

Obstetrics professionals receive training offered by the Cord Blood Banks (hereafter CBBs) and completed by the use of the e-learning platform made available to them by the ABM.

The medical contraindications to cord blood donation and the mother's health questionnaire are integral parts of the training provided to midwives (in a document prepared by the RFSP and validated by the Agency's Medical and Scientific Council, CMS).

This information covers the benefits expected from this type of donation for patients wherever they are in the world, the collection procedure, the potential risks, the testing of maternal and cord blood samples, and the procedures for the qualification and storage of cord blood. It also considers compliance with the laws protecting personal data.

Pregnant women are informed of their right to change their mind and not proceed with this donation at any time before delivery.

Cord blood donation is voluntary, anonymous and is a free gift. Before delivery, at an antenatal visit, pregnant women who have accepted the principles of this donation sign an informed consent form[13] reviewing all of the essential information associated with cord blood donation and validated by the ABM.

Donors are also informed that any event happening to their child after their cord blood has been donated which present a potential contraindication to the use of this graft must be communicated to the CBB, either by their doctors or by the mothers themselves.

[13] Informed Consent Form for cord blood donation, produced by the RFSP and ABM in 2010, updated in 2023

2- Registration of new cord blood units in the database of the French unrelated stem cell donor registry (FGM)

2.1 Quality criteria for the registration of new cord blood units

National CBBs receive from their maternity partners both the collected cord blood and maternal blood samples for required testings. The characteristics of these samples are recorded on a collection form, which includes all of the details related to the delivery, the date and time of collection, and the child's sex.

At this stage the cord blood samples considered to meet requirements for processing are those with a volume ≥ 80 ml.

The maternal blood samples enable the performance of relevant quality control including:

- the HLA class I typing necessary to link each mother to the Cord blood Unit (hereafter CBU) associated with her
- the regulatory infectious disease markers testing necessary to the indirect biological qualification of the CBU.

The stages below describe the set of laboratory and clinical data that characterize the CBU for its registration on SYRENAD.

2.1.1 Cell count

For every compliant collection, the national CBBs perform viability testing and TNC count, in order to ensure that the unit's cell count corresponds to the expected quality criteria.
The TNC threshold defined by the RFSP for the registration of a new CBU- post reduction of the product- is $160x10^7$.

2.1.2 Infectious disease markers

The infectious disease markers required for the biological qualification of a CBU and its registration are tested from a maternal blood sample collected at delivery.

The list of infectious disease markers is based on the relevant regulations in force and included in the RFSP documentation, provided to all CBBs.

2.1.3 Necessary samples

When a new CBU is registered, maternal samples and cord blood samples (serum/plasma and DNA) must be kept available for subsequent additional testing.

2.1.4 HLA Typing at registration

The ABM defines the extent and the level of resolution of the HLA typing to be performed as part of the national strategy.

The minimal HLA typing strategy for CBU registration is defined as follows: HLA-A, B and C loci at intermediate/high resolution (DNA based typing), DRB1 at high resolution/allelic level (DNA based typing).

The initial HLA typing, extended typing, and confirmation/verification typing are all performed by an EFI-accredited histocompatibility laboratory, associated with the CBB.

The DNA must remain available for subsequent HLA typing (extended or verification).

2.1.5 Postnatal clinical qualification

To be able to register a new CBU, the CBB must have received a postnatal clinical qualification of the newborn (performed at least 6 weeks after the delivery).

2.2 Effective registration of cord blood units

CBUs intended to registration in FGM Cord Blood Registry must meet the regulatory requirements as well as the quality criteria defined by the RFSP[14].

The labelling and processing of the collected CBUs must be performed in accordance with rules of good practice.[15],[16]

All CBUs are registered in SYRENAD by CBBs, which attribute an anonymous identification code unique to each CBU.

The CBBs record all the characteristics useful to transplant physicians for preselecting and even selecting a CBU (in accordance with the CBU characteristics form/CBU report: HIV, HBV, HCV, HTLV, CMV, EBV, syphilis, toxoplasmosis and any other infectious agent, according to the mother's travel history and changes in relevant regulations, as well as ABO and RH blood groups and hemoglobin electrophoresis).

In the case of abnormalities for one or several infectious disease markers or any other biological or clinical abnormality, the director of the cord blood bank duly informs the mother in writing that the CBU did not meet standards, as well as the referring midwife and/or the mother's general practitioner, who will also be informed of the cause of the non-conformity. An additional medical evaluation of the mother or new-born may be required.

The medical questionnaire completed for every CBU registered on SYRENAD includes the family medical history and potentially any known genetic abnormalities of the father and mother, the mother's travel history, and the course of the pregnancy and delivery.

The cord blood donation at birth is mentioned in the child's health notebook by a sticker with the CBB's contact information.

Moreover, the parents are told both before and after the donation of the importance of reporting any disease happening to the child at any time after the donation.

The CBUs registered in SYRENAD are visible and accessible, both nationally and internationally (via EMDIS and EMDIS-CORD) for any patient.

3- Response to a request for additional testing or biological samples

The requests for further testing received by the FGM registry can be for:

- an extended or confirmatory/verification HLA typing;
- Serologic tests to screen for infectious disease markers;

[14] Form: CBUs characteristics according to RFSP

[15] Decision dated 5 May, 2017, modifying the decision of 27 October, 2010, defining the good practice rules for tissue cell preparations for cell therapy

[16] ANSM decision dated February 7, 2020, defining the good practice rules for the collection of human body tissue and cells from a living or deceased person, for therapeutic use

- A request for biological samples.

The FGM registry verifies the conformity of the request and transmits it to the CBB concerned.

If this request comes from a registry connected to EMDIS, it is transmitted to the CBB directly in SYRENAD (search phase).

3.1 Reservation of a CBU

Further to any additional test request, the CBU is automatically reserved for the given patient until results are provided.

FGM strongly recommends that CBBs carry out the requested testing onsite, to avoid any lack of biological material.

If onsite testing is not possible, the CBB informs FGM and organizes the shipment of the biological samples necessary to carry out the testing requested to the laboratory(ies) of the TC:

- Biological samples must be anonymized and labeled accordingly.
- They must be packaged in a secured box provided by the ABM, in accordance with IATA requirements[17].
- They must be shipped to the address communicated by the TC, by the transport company which the ABM has signed a contract with.

3.1.1 Reservation with or without HLA typing request

A CBU is reserved for a 2 months period upon simple request from the TC, with or without a HLA typing request.

At the end of this period, a request to extend the reservation is possible for a maximum duration of 1 month. Beyond that period, the renewal of the reservation can only be granted once, after validation of the TC clinical arguments by the medical team of the FGM registry.

In any cases, without request for extension of the reservation or without CBU formal recruitment, the CBU is released at the end of the reservation period and available again for any patient.

In case of any additional HLA typing request, the CBB carries out the HLA typing and enters it into SYRENAD. The entered results must comply with the level of resolution requested by the TC. If this is not the case, this testing cannot be invoiced.

As part of its WMDA accreditation, FGM registry must apply and see applied the WMDA quality standards; the WMDA recommends that 80% of high resolution typing be carried out within 14 days[18] of receipt of the request.

In case of any urgent request, typings must be performed within 7 days of receipt of the request.

[17] http://www.iata.org/whatwedo/cargo/dgr/Pages/index.aspx

[18] WMDA Key Performance Indicators for Registries ; 10052022-WGQR-KPI 2021

4- Formal recruitment of cord blood unit

The formal request for a CBU is made by a French TC or by an international registry.

The CBB responsible for the management of the recruited CBU, is informed by FGM. Together they organize the entire process for the validation and shipment of the CBU.

This CBU is formally reserved for the intended patient.

At this stage, TC can request DNA.

DNA can be sent by the CBB :

- either before the CBU is shipped, using the services of the courier company under contract with the ABM

or

- at the same time of CBU shipment, placed in the dry shipper.

The CBB confirms the shipping date, the CBU's local codes and the bag integrity by returning the dedicated form to the FGM registry CBF/CBI002 “CBU pre-release verification”. This document is then transmitted to the TC.

4.1 Selection of cord blood units

4.1.1 Minimum criteria for selecting a cord blood unit for a recipient

The minimum criteria for the selection of a CBU are the HLA compatibility and the number of TNC and CD34+ cells.

The SFGM-TC (the French-speaking Bone Marrow and Cell Therapy Society) recommends that national transplant centers take into account the HLA A, B, C and DRB1 loci, at a high or allelic level of resolution and avoid insofar as possible any DRB1 mismatch.

The SFGM-TC also recommends that national transplant centers choose for a single unit transplant a minimum number of TNCs $\geq 3x10^7$/kg and of CD34+ cells $\geq 1x10^5$/kg (recipient's body weight), before thawing.[19]

[19] Form: CBUs characteristics according to RFSP

4.1.2 Final selection of a national cord blood unit

The FGM registry coordinates the process of CBU recruitment and shipment, working with the CBB and the national TC or international registry.

Recruitment pages (Master Request Form), signed and dated by the transplant physician, are received by email at the FGM registry.

On receipt, the information is reviewed by the FGM registry coordination, validated by a physician, and transmitted within 24 h to the CBB, by email.

The CBB ensures the integrity of the bag(s), as well as the match between the CBU registration ID and the bag(s) ID.

Quality control is required before the CBU is released, as well as verification typing to confirm its identity, performed from a contiguous segment, attached to the bag.[20]

If the hemoglobin electrophoresis was not performed at the time of the registration, this must be done before shipment. The result must be available at least 48 h before the CBU is shipped (except if the CBU is urgently expected).

The signature of the CBB director on the CBU report also attests that all of the documentation available has been reviewed, including the medical questionnaire, the postnatal check-up data, and all other relevant biological and clinical elements

The CBB, working closely with the FGM registry, then arranges the CBU shipment to the TC.

4.1.3 HLA typing at the time of release

The identity confirmation typing is performed on a different sample than the one used for the initial HLA typing.

If a discordance in the typing appears, the FGM registry must be immediately informed. The TC can then decide to continue or release the recruited CBU.

FGM annually transmit the discordant typing cases to the WMDA "HLA discrepancy" study group.

For the oldest CBUs, which may not have a contiguous segment attached to the bag, the CBB must have a procedure in place to confirm the identity of the unit before shipping. The FGM registry must inform the TC/international registry of this before the CBU is shipped.[21]

5- Shipment of cord blood units

5.1 Transport organization

Transportation arrangements are made jointly by the TC, the FGM registry, the CBB, and the transportation company.

[20] Fact-Netcord Standards (7th edition) E 3.2 and 5.1.1 (guidance)
[21] Fact-Netcord Standards (7th edition) E 3.2.4

French CBBs are only transported by the transport company which is contractually bound to the ABM

This contract includes an obligation for the company to have a specific insurance policy covering any damage or losses that might occur in transit.

Indeed, if the transportation material (dry shipper and/or its protective packaging) is damaged during transportation, or if the CBU is made unusable for the transplant, the insurance of the transport company must compensate the ABM for the loss of the material and/or the cost of the CBU.

In the case of export toward a third country (non member of the EEA), the CBB must obtain export authorization from the French National Agency for Medicines and Health Products Safety (hereafter ANSM) before the CBU is released. Exportation without authorization is subject to prosecution.[22]

The CBB must ensure that the transport company meets the conditions required to provide satisfactory management and transportation of the CBU.

Every measure must be taken to enable the CBU to be shipped as quickly as possible, depending on the travel distance, and in any case, within less than 72 hours.

The shipping company is responsible for transporting the CBU from the CBB to the TC.

The CBB must make sure that the transport documents are complete and attached to the CBU.

The documentation includes:

- The complete sheet of the CBU's characteristics, dated and signed by the CBB medical director,
- The thawing procedure,
- The FGM CBU collection/delivery fom (CBI023),

Any other document that could be demanded.

A dry shipper can contain only one cord blood unit.

Two CBUs from the same CBB recruited for the same patient can be shipped together, only if previously agreed by the transplant physician.

The FGM registry recommends photographing the bags before placing them in the dry shipper.

5.2 Care of dry shipper

The CBU is transported in a dry shipper provided and packed by the CBB, equipped with a temperature monitoring probe that traces the interior temperature of the dry shipper throughout the entire journey. The temperature must not exceed -150°C. [23]

The dry shipper must have reached the desired shipping temperature at the moment the graft is placed in it to start the journey.

The dry shipper is placed inside an outer protective container.

The transport company shall ensure that the secure containers have attached or applied to them the following items:[24]

[22] Public Health Code Article L1245-5 and L1272-8 and Penal Code article 511-8-2

[23] Fact-Netcord standards (7th edition) E 5. 3

[24] Fact-Netcord Standards (7th dition) E 5.3.3 and E 5.3.4

- labels which explain the requirement for a strictly vertical position, the nature and fragility of the product transported,
- Shock indicators,
- Tilt and mishandling indicators.

Dry shipper must also be sealed or padlocked.[25]
- If it is sealed, the seal will be traced,
- If it is padlocked, the combination for opening must be addressed separately to the person receiving the dry shipper at the TC.

The courier must have a spare seal, in case the container must be opened during transport (at the request of customs officials). The spare seal must be requested to the CBB responsible for the release of the CBU.

If used, the spare seal will also be traced on the documents (number, time).

5.3 Transport of the cord blood unit

Transport is usually done by route, train, or airplane (depending on the distance).

The interior temperature of the dry shipper must be recorded throughout the entire trip.[26]

The dry-shipper/CBU must in no case be irradiated when it goes through the airport security area.

The secured dry shipper must always be transported vertically, regardless of the means of transportation. To prevent the dry shipper being turned upside down when sent by air, the shipper must attach it to a shipping rack.

Each time a new person becomes responsible for the dry shipper during transport, both parties must re-verify the shock and tilt indicators and the integrity of the dry shipper.

This verification must be traceable (either on paper or electronically).

The secured dry shipper shall imperatively be delivered personally into the hands of the recipient indicated on the transport document or a person duly authorized by the TC or international registry. The courier must have signed the CBI023 FGM form "Transport document-Human product for therapeutic use", attesting to the delivery of the CBU.
On receipt of the CBU, the cell therapy unit at the TC must confirm the integrity of the bags and complete and sign the CBI023 FGM form.

Once released, the CBU cannot be returned to its original CBB.[27]

In cases of damage, the transport company shall take photographs of the container and/or of the dry shipper and/or the applied indicators and transmit them, together with an incident report, to the FGM registry, as rapidly as possible.

[25] Fact-Netcord Standards (7th edition) E 5.3.5
[26] Fact-Netcord Standards (7th edition) E 5.3.1
[27] Fact-Netcord Standards (7th édition) B 9.5.1 and E 6.5

6- Correspondence between the CBU donor and the recipient

According to RFSP recommendations, no exchange of correspondence between the parents who have accepted the donation of their child's cord blood and the recipient is authorized.

7- Anonymity

The personal data of the parents and/or child must not appear on any document sent between the CBB and the TC.

The CBU must always be mentioned by its identification code as assigned by the SYRENAD..

8- Record retention and archiving

The data of both mother and child are stored in a totally secure manner at the CBB for the entire period of CBU storage, in accordance with the procedures and regulations in force and are not made available for CBU searches, but only for inspection or assessment.
The complete files of mothers and children are archived for 30 years, in case of transplants performed with these CBUs.[28,29]

[28] Decision of the DG of the ANSM of February 7, 2020 defining the rules of good practice relating to the collection of tissues and cells from a living or deceased person, for therapeutic use

[29] Article R1112-7 of the Public Health Code

Registration of national and international patients for donor search and management of stem cell collection requests through the national FGM Registry

PATIENTS RECEIVING AN HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM UNRELATED DONORS

1- Search for unrelated HSC donors

The FGM Registry, as part of the ABM, is the only institution allowed to perform unrelated donor search on behalf of transplant physicians working in hospitals authorized for HSC allotransplants.

The search for an unrelated donor is initiated at the request of a transplant physician, by a search unit (local histocompatibility laboratory), which liaises with both the TC and FGM and uses the dedicated management software, SYRENAD, provided by FGM.

This search begins by registering the patient into SYRENAD.

1.1 National Patients

1.1.1 Patients registration

The FGM form CF001 (“registration form”) for patient registration, must be completed, validated, and co-signed both by the transplant physician and by the head of the histocompatibility testing laboratory that performed the patient's HLA typing. The administrative department of the TC issues a purchase order attesting its financial commitment for the patient's registration on the national registry, the search for unrelated donors, and the provision of an HSC graft, when available.

In all French TCs, the indication of an HSC allograft is discussed and validated by a multidisciplinary committee. This procedure is mandatory for all TCs (see decree DGOS/SDO/2005/101 dated February 22, 2005).

The patient's diagnosis must be mentioned on the current list of indications, validated by the French Bone Marrow and Cell Therapy Society (SFGM-TC) and the European Group for Blood and Marrow Transplantation (EBMT). This list is included in the CF001 (“registration form”). If the diagnosis is not mentioned on this list, the registration request is then reviewed by one of the physicians at the FGM registry, together with expert physicians from the SFGM-TC, if necessary.

The FGM registry coordinators verify the completeness of the form CF001 upon reception and enter the data into SYRENAD within the next 24 hours.

If the form is incomplete, the coordinators send a request for additional information to the search unit of the TC.

The registration information entered by the coordinators is transmitted in real time via SYRENAD to the transplant search unit, responsible for verifying it, correcting it if necessary, and validating it before the search process can begin.

The HLA typing at the time of registration must be performed at least at intermediate resolution level for the HLA-A, -B, -C, DRB1, and DQB1 loci and the DPB1 locus if available. High-resolution/allelic HLA typing (minimum 4 digits, without ambiguity) is nevertheless strongly recommended in order to facilitate and speed up the search, and is required for the selection of an unrelated donor or a unit of placental blood (USP) for transplant.

1.1.2 Search for unrelated HSC donors

Searches are performed according to the search algorithm defined by the FGM registry, taking into account the level of HLA compatibility requested by the TC.

Once the TC search unit has validated the registration, this launches a nationwide search. The TC search unit can immediately conduct the search internationally, through the choice of registries listed on EMDIS. EMDIS is the international communication system linking partner registries worldwide.

The international registries to be searched can be selected after consultation of the WMDA "Search and Match" database, made available in SYRENAD. More specifically this database provides the list of the HLA characteristics of all unrelated donors registered in registries around the world.

SYRENAD performs real time automated searches for donors in France, and 5 times a day across the world in the registries connected to the EMDIS international communication system. A search report is immediately generated and sent automatically to the transplant search unit.

Exchanges with registries not connected to EMDIS are done by email. SYRENAD automatically generates the initial or preliminary search request form, which is sent by the FGM coordination team to the appropriate registries, which respond by generating and sending a search report.

A donor search update can be performed directly on SYRENAD for national donors and connected international registries, or requested in writing to non-connected registries. In this case, the FGM coordination team receive this update from the non connected registries and transmit it to the TC search unit.

1.1.3 Request for complementary testings

These requests may occur for extended HLA typing (typing of additional loci or subtyping at a higher resolution level), for verification typing, for screening tests for infectious disease markers, or for blood samples shipment.

The HLA verification typing must always be performed before the work up request. In urgent cases, the HLA verification typing can be performed after the work up request, but before the start of patient's conditioning.

These requests are sent by the French TC search units:

- To national DCs and/or to international registries connected to EMDIS, directly via SYRENAD;
- To international registries not connected to EMDIS, via the FGM coordination team using the FGM or international registry standard forms.

In case of blood samples request, the TC search unit is informed of the date the samples are shipped:

- via SYRENAD for national donors and for international donors registered on an EMDIS-connected registry;
- via email sent by the FGM coordination team, for international registries which are not connected to EMDIS.

If testings are performed by the DC, the results are made available in SYRENAD:

- once submitted by the national DC;
- via EMDIS, if the donor is registered on an international EMDIS-connected registry.

  If the international donor is registered in a registry not connected to EMDIS, the results are transmitted by the FGM registry coordinators by email.

Following a request for complementary tests, the national donor is automatically reserved, and his change of status can be consulted in SYRENAD. The duration of the reservation varies according to the type of request, from 3 to 8 weeks.

If the requested donor is already under consideration for another patient, the FGM coordination team ask the TC in charge of the initial patient to decide about maintaining or cancelling the reservation.

If the donor-national or international- is eventually not selected for the considered patient, the TC search unit must discard the biological material received from this donor.

1.2 International patients

1.2.1 Registration and searches

The patient's diagnosis is the only criteria assessed by FGM registry and the list of accepted diagnosis is made available in "WMDA Share".

The diagnosis must be mentioned on the current list of indications, validated by the SFGM-TC and the EBMT. If this is not the case, the registration request must be reviewed by one of the FGM registry physicians.

Connected registries:

The patient registration is received via EMDIS, containing the list of accepted diagnosis, approved once for all. The search report is immediately generated and automatically transmitted to the international registry at the next EMDIS connection (frequency = 5 times/day).
The international registry is free to repeat the search and thus receives, via EMDIS, updates on national donors.

Non-connected registries:

The international registry sends its own registration request form by email.
The FGM coordination team register the patient into SYRENAD, run the search and then print out the search report, which is then sent to the international registry.
Searches are repeated upon request.

1.2.2 Request for complementary testings

Connected registries:

The international registry sends its requests for complementary testings via EMDIS. The national DC receives them directly by SYRENAD and performs the tests.

The date of sample shipment and/or test results performed at the national DC, are submitted by the DC into SYRENAD and thus sent automatically to the international TC, via EMDIS.

If the international TC performs itself the tests, using a donor blood sample, results have to be sent via EMDIS and the national DC receives them directly in SYRENAD.

Non-connected registries:

The international registry sends its requests to the FGM registry coordinators, who submit them in SYRENAD for automatic transmission to the appropriate national DC

When blood samples are requested, the national DC submit the shipment date into SYRENAD, and FGM coordination team transmits this information by email to the International registry.

If the complementary tests are performed by the DC, the FGM coordination team, retrieves the results from SYREAND and by email to the international registry.

If the international TC performs itself the tests, using the blood sample previously received; the results must be sent by email to the FGM coordination team, in charge of transferring them to the concerned DC.

Following the reception of a request for complementary tests, the national donor is automatically reserved for the patient, and his change of status can be consulted in SYRENAD.

The duration of the reservation varies according to the type of request - 3 weeks following a complementary HLA testing and 8 weeks following a blood sample shipment.

If the requested donor is already under consideration for another patient, the FGM coordination team ask the TC managing the initial patient to decide about maintaining or cancelling the reservation.

A donor is systematically reserved from the workup request until workup termination.

2- HSC donors recruitment

2.1 Recruitment of an HSC donor for a first donation

The TC search unit recruits the main donor selected.

At this stage, the TC search unit ensures that at least 1 back-up donor has been identified and available. The backup donor can be recruited in parallel with the main donor to secure the transplant project

2.1.1 Recruitment of a national or international donor for a national patient

The TC search unit enters the data relating to the formal recruitment of the compatible donor directly into SYRENAD/EMDIS.

The forms needed for the workup request must be dated and signed by the transplant physician and then sent to the FGM coordination team by email.

The workup forms are reviewed by an FGM registry physician and then transmitted by email by the coordinator to the appropriate national DC or international registry, which confirms both, request reception and donor availability.

The FGM coordination team liaise the organization of the workup together with the concerned national DC or international registry, and with the national TC. FGM coordination team is the unique functional and operational interface, and thus is the warrant of the strict respect of donor/recipient anonymity.

In case of bone marrow collection request:

The donor is seen in consultation by a hematologist from the local transplant/collection center. The hematologist validates the prescription done by the transplant physician via the "Verification of Prescription" form or proposes a new quantity of cells to be collected, if the quantity of cells requested appears to be inadequate with what it seems possible to safely collect from the donor.

In case of discrepancy between the quantity expected by the transplant physician and the one which is likely to be collected, the transplant physician has to make the decision:

• Accept a reduced quantity of cells;
• Change HSC product;
• Cancel the request. In that case the whole workup is cancelled.

The donor is also seen in consultation by an anesthesiologist who will validate his ability to receive general anesthesia for this type of collection

In case of PBSC collection:

The donor is seen in consultation by a hematologist from the local transplant/collection center, who validates his ability to make this type of donation and prescribes the growth factors that will be necessary for the mobilization of the hematopoietic stem cells.

The donor is also seen by a physician in charge of the apheresis to be performed, in order to definitively validate the prescription requested by the transplant physician.

The estimated amount of cells to be collected and the estimated number of cytapheresis (2 session maximum) are communicated to the transplant physician before the start of the patient's conditioning.

A pre-collection sample is requested by the TC, to perform as follows and within the legal period of 30 days:

- The verification of donor HLA typing, to confirm the donor center's initial HLA typing, when applicable;
- Any complementary infectious disease markers (IDMs), when applicable.

The mandatory IDMs for validating a donor's final suitability for HSC donation are defined by decree and published in the "Journal officiel de la République".

The following infectious disease markers[30] must be tested, by the DC- or the TC if appropriate- in the 30 days prior collection date:

- Syphilis serology;
- HBs antigen;
- Anti-HBc antibodies: → if positive, screening for anti-HBs antibodies is required;
- HBV PCR;
- Anti-HCV antibodies;
- HCV PCR;
- Combined test for anti-HIV1 and HIV2 antibodies and p24 antigen;
- HIV PCR; → If it appears impossible to perform the PCR or if the results cannot be provided in time before transplant, isolated p24 antigen testing must be performed, as well as the combined test;
- HTLV1-V2 antibodies;
- Anti-CMV antibodies (IgG or IgG + IgM);
- Ant-EBV antibodies (IgG anti VCA or IgG anti EBV);
- Anti-toxoplasmosis antibodies (IgG or IgG + IgM);

Depending on the conclusions of the medical consultation and the possible exposure of the donor to specific infectious agents, the followings additional tests can be performed:

- additional PCR (DGV) on the 3 markers HIV, HBV, HCV, to be carried out before the start of the patient's conditioning – For any situation at risk of infection occurring in the 4 months preceding the date of collection of CSH.
Result must be available at least 24 hours before the start date of conditioning.

- Chagas disease, Nile virus, Malaria, Chikungunya, Zika, Dengue, SARS-CoV-2, TBEV... or any other infectious marker, in accordance with the recommendations issued by the HCSP.and following a stay in areas at risk of infection.

The medical consultations and laboratory tests required must be arranged by the DC.

The TC must get all the results before the start of patient's conditioning.

The results are valid for 30 days from the date of sample collection. After 30 days (e.g., if the collection is delayed), all of the tests must be performed again using a new blood sample from the donor.

If an international donor is recruited:

[30] Decree dated June 22, 2011, concerning the methods for medical biology analyses to test for infectious disease markers in human body parts and products collected for treatment purposes, except for gametes, blood, and blood products, supplemented by the ANSM 2013 Recommendations

The FGM registry must communicate the list of mandatory infectious disease markers[31] required for the biological qualification of a donor to the appropriate international registry.

If one or several markers cannot be tested by the international DC, a blood sample from the donor must be sent to the TC.

There are acceptable alternatives if the following required PCR results are absent:[32]

- If the PCR for HIV cannot be performed, screening for the isolated p24 antigen has to be done;
- If PCR for HBV and HCV cannot be performed, the donor must be qualified using the other required viral markers.

If the patient's clinical status worsens in the days before the scheduled transplant date and therefore before the donor stem cell collection, the transplant physician must immediately inform the FGM registry, either the coordinators in charge or the physician on call after office hours (emergency contact telephone number available). The FGM registry transmits this information to the concerned international registry/donor center via the CI070 “Notification of critical information” form, which has to be returned duly signed by the corresponding DC/Registry/ in order to attest good reception of the information.

2.1.2 Recruitment of a national donor for an international patient

A national donor is recruited for an international patient via SYRENAD/EMDIS for the connected registries, or by email for the registries that are not connected.

The recruitment process follows the same stages as those described above for a patient in France.

2.2 HLA compatibility criteria between donor and recipient

The HLA compatibility criteria, required for the formal recruitment of a donor for HSC donation, relate to the HLA antigens A, B, C, DRB1, DQB1, even DPB1, at high resolution/allelic level (DNA based typing). A minimum compatibility level of 9/10 HLA antigens is accepted.
Any project to recruit a donor with a donor/recipient compatibility level of less than 9/10 must be justified and argued by the transplant physician (minutes of the multidisciplinary consultation meeting – RCP, for example). Consultation from an expert committee will be requested by the FGM registry.

2.3 Recruitment of an HSC donor for a second or additional donation

2.3.1 Recruitment of a national donor

After donation, the HSCs donor’s status is changed and becomes " unavailable" for new donor searches. This status change is implemented in SYRENAD by the DC. The donor remains available for the same recipient only, in case a second donation is needed.

This second donation can be a BM, a PBSC, or a lymphocytes donation (DLI). It may be performed (with some exceptions) over a variable period that may range from one month to several years after the first donation.

[31] Decree dated June 22, 2011, concerning the methods for medical biology analyses to test for infectious disease markers in human body parts and products collected for treatment purposes, except for gametes, blood, and blood products supplemented by the ANSM 2013 Recommendations
[32] Decree dated June 22, 2011, concerning the methods for medical biology analyses to test for infectious disease markers in human body parts and products collected for treatment purposes, except for gametes, blood, and blood products supplemented by the ANSM 2013 Recommendations

A second donation of PBSC, by a donor who has already given PBSC at first donation for the same patient is possible (ref. decision of the medical and scientific committee of the ABM dated November 9, 2021) .
It may be carried out after donor consent and medical validation.

Donors who gave BM as a first donation can be requested for a second BM, PBSC or DLI donation.

If needed, a second session of DLI can be performed, at least one month after the date of the first donation, and after donor consent and medical validation.

All requests for a second donation must be submitted using the form CF021.6 “WMDA previous transplant history and formal request for subsequent HSC collection”. Upon reception, this form is reviewed by an FGM physician before transmission to the donor center. The procedure for the donation request is then the same as for the request for a first donation.

2.3.2 Recruitment of an international donor

All requests for a second or additional donation must be justified by the concerned registry using the form CF021.6 “WMDA previous transplant history and formal request for subsequent HSC collection”.

The procedure for a second donation request is then the same as for a first donation.

2.4 Conditions for HSC cryopreservation

The cryopreservation of the entire collected HSC can only be considered on the basis of a formal request, with supporting arguments, coming from the TC, with the joint agreement of the registry, the donor center, and the TC.

The donor must be informed of the planned cryopreservation.

The transplant physician must specify the presumed date of infusion before the collection and cryopreservation of the HSCs occur.

Cryopreservation of the entire collected HSC product can only be requested, as an exception, in the following situations:

- When the donor is unavailable on the proposed collection dates and the transplant cannot be delayed;
- When a clinical complication occurs to the patient, but does jeopardize the planned transplant;
- When only one source of stem cells can be collected (no additional collection possible).
- When the sanitary context make the collection on the fixed date hypothetical
- When transport critical conditions make the delivery of the product on the expected date uncertain

Once delivered at the TC, product is cryopreserved by the cell therapy laboratory associated with the TC. In case of a critical situation (duration of transport, contingencies related to transport), the product can then be cryopreserved upon agreement by the cell therapy laboratory of the collection center
Cryopreservation of a fraction of the collected HSC product is possible when the collection has generated more TNCs/CD34+ cells than expected. This information must be communicated to the FGM registry using the Quality Control form, issued by the TC's cell lab.

As soon as infusion has been performed, the physician must inform FGM, so that the DC or the international registry can in turn be notified.

3- Transportation of HSC (bone marrow and PBSC) and DLI

3.1 Preamble

The transportation is made in compliance with:

- The provisions of the Public Health Code and especially articles L 1245-2 and R.1245-1 *et seq* related to the import and export of organs, tissues and their derivatives, human body cells and products of gene and cell therapy, and modifying the Public Health Code.
- The decision dated October 27, 2010,[33] approving the regulation concerning good transportation practices for collections, products, and samples of human blood as well as good practice rules concerning the processing, banking, transportation, selection, and release of tissues, their derivatives, and cell therapy products, called for by article L 1245-6 of the Public Health Code.
- ANSM document of October 2012 concerning the transport conditions of HSC and MNC from the collection site to the cell therapy lab.
- ANSM decision of May 5, 2017, modifying those of October 27, 2010 concerning labeling of the product in compliance with European regulations (single European code - SEC)
- Guidelines of good practice for collection of HSC, of February 7 2020
- The WMDA recommendations: Guidelines for couriers and transportation of hematopoietic progenitor cells (20210609-EQ.P.Courier Guidelines).

3.2 Organization of transportation

The TC is responsible for organizing the transport of the collected product.
He assigns a transport company which he signs a contract with. This company can be chosen from the list proposed by the UNIHA platform, after competition between companies, Alternatively TC can assign hospital staff trained for this purpose.
Transport coordination is carried out jointly by the TC, the associated cell therapy laboratory, the transport company (if applicable), the donor/collection center and FGM registry.

The cell therapy lab affiliated with the TC, must validate the transport route proposed by the courier company and must approve the arrangements and conditions for the transport (impact on the quality of the graft).

Every measure must be taken to enable the HSC to be transported as rapidly as possible, depending on the travel distance and in any case, within less than 72 hours after the collection began.

In case of international HSC exchanges with third countries (i.e. countries not members of the European Union), an authorization for import/export, as applicable, must be requested and obtained

[33] ANSM decision of October 27, 2010

from the ANSM by the cell lab of the TC, before the start of patient's conditioning. The lack of authorization is subject to prosecution.[34]

This authorization is not required for exchanges within Member States of the European Union or of the European Economic Area (EEA).

The transport documentation:

The transport documentation is prepared by FGM upon receipt of form CF019: "Courier details" - for a mission abroad, sent to the FGM registry by the transport company assigned. This form must be sent one week before the carrier's departure date.

The FGM registry electronically edits transport documents to facilitate the graft's transport and transit. The file, made of all official documents that must be presented to airport/border authorities, concerns the product being transported. This file contains:

- A cardboard label, to be attached to the external container, mentioning the donor code and the contact details of the CC and TC;
- A set of courier nominative documents, together with the forms to be completed by the CC.

The documents provided by FGM are sent by email to the transport company or to the TC- in the case of an international donor for a national patient or to the DC in the case of a national donor for a national patient.

These documents must be printed upon receipt and made available to the courier before the start of his trip, in order to be presented to the collection center when the collected product is picked up, then to airport security when the product is transported.

The transport container:

It is essential for the courier to arrive at the donor/collection center with a qualified isolated container provided by his/her courier company, that ensures the maintenance of the temperature set, as validated by the TC's cell lab, in compliance with the good transportation practices established by AFSSAPS on October 27, 2010, modified by ANSM on May 5, 2017. It is mandatory that this container is equipped with a recording system, able to track the temperature throughout the journey.

The container must be kept at the transport temperature required by the cell therapy lab, at the time the graft is taken in charge, in accordance with good national practices issued by the ANSM.

3.3 Transportation of the HSC

Transportation takes place normally by train or airplane (depending on the distance) and rarely in a car. The person responsible for the transport cannot transport the graft alone in a private car.

In case of air transportation:

The FGM registry contacts 24 hours in advance, by email:

- The national airport authorities:
  - to alert them of the import or export of cells of human origin for transplant
  - to allow the airport personnel to facilitate the escort's mission.

The courier must:

- Indicate to the airline company, at the time of ticket reservation, that human HSC for transplantation are being transported. The type of transported product will be associated to the passenger's name (PNR, passenger name record) in the airline's computer records.

[34] Public Health Code: Article L1245-5 and L1272-8 and Penal Code: article 511-8-2

- Go to the customs area upon arrival at the airport to report that human HSC for transplantation are being transported. In case of problems or incidents, the courier can contact the FGM registry coordination team or, outside office hours, the FGM physician on call using the emergency phone number, or, the Agency's national organs regulation unit (PNRG).
- Make every effort to prevent the container containing the HSC from exposure to X-rays. The cells must in no case be irradiated at the airport security area as this could damage their quality. The product can be shown to and handled carefully by the airport authorities, using the surgical gloves available in the container for this purpose. The empty container can go through the X-ray machine. It must never be placed in the luggage compartment of the airplane, but on the floor in front of the courier seat.

In case of rail transport:

- The FGM registry does not systematically alert railroad authorities, unless the trip concerns international transportation (e.g., Eurostar, Thalys).
- The courier is advised to alert the train staff in order to inform him or her of the nature and importance of the product being transported.
- The container must remain with the courier at all time and must not be placed in a location accessible to other passengers.

Any incident having a possible impact on the quality of the HSC has to be communicated to the TC and, for information, to the FGM registry. FGM can generate a biovigilance report, if applicable.

3.4 Courier profile

Most of the time the HSC are transported by a person duly designated and hired by a courier company missionned by the TC, or transported by a member of the TC staff.

In view of the unique nature of the cells, the courier must have successfully completed a specific training course dedicated to the transport of HSC or MNC products, conducted by the ABM (https://www.agence-biomedecine.fr/Les-formations) in compliance with the WMDA quality standards.

The courier is responsible for the transportation of the cells from the collection site to the TC's cell lab site.

The courier assigned must:

- Not have any conflict of interest with the patient and/or the donor;
- Have experience of the various modes of transport, nationally and internationally
- Be exclusively dedicated to the transportation of the HSCs/MNCs from the consignment of the cells until their delivery to the TC);
- Have a passport, valid for 6 months after the return date, or a national identity card currently valid at least until the return date;
- If necessary, have obtained in advance an entry/exit visa for the country concerned;
- Not register his luggage to save time at the airport.
- Never be separated from the HSCs, for any reason, for the entire duration of the transport;
- Have a sense of responsibility and of initiative, allowing him/her to cope with any unexpected situation;
- Speak English fluently in the context of international transports;

- Have an international credit card with sufficient funds;

- Be reachable throughout the mission and therefore be equipped with a cell phone accessible at any time in the geographic areas concerned;

- Have the telephone numbers of the main contacts concerned (cell therapy lab/TC, transport company supervisor, FGM registry and emergency number of the physician on call) to be able to alert them in case of an emergency or in case of any potential incident occurring during the trip (in either direction);

- Strictly maintain donor/recipient anonymity (see Bioethics law of July 1994, revised in August 2004, in July 2011 and then in August 2021, and the European General Data Protection Regulation 2016/679) and refuse any letter or gift, from either the collection center or the TC that might compromise this anonymity (see donor/recipient correspondence).

- Keep with him/her the nominative documents issued by the FGM registry, which attest of his/her mission. When passing through customs, the courier has to provide all the necessary documents to justify his/her identity and mission;

- Make every effort to prevent the transport container from exposure to X-rays.

- Communicate any information about modification of the transport plan or occurrence of an incident, to the TC, his/her company, the CC if necessary, and the FGM registry.

- Take all necessary steps for the HSCs to be delivered in the shortest possible time.

3.5 Pick up and delivery of HSC product

The FGM registry recommends that the courier arrives in the city, where the HSCs will be collected, on the day before the collection.
However:

- for a PBSC collection-either national or international collection- an arrival on the day of the first session is possible, under prior agreement of the CC;

- for a BM harvest, the courier must arrive the day before the collection, when the collection center is international, but can arrive the same day when the collection occurs in France, under prior agreement of the CC;

In all cases, the courier must be physically present before the time of the scheduled delivery of the cells by the CC.

Upon arrival in the location of cells collection, the courier must inform the CC of his/her safe arrival and check the time of the cells delivery.

If the delivery is delayed to the next day, the cells must be stored at the collection facility or at the donor center or cell lab, under appropriate conditions, and then handled over to the courier on the day of travel;

The cells must never be stored in an hotel room refrigerator, except under exceptional circumstances duly justified and always under agreement of the cell lab of the TC and the FGM registry. In this case, the courier cannot leave the hotel room.

Upon arrival at the CC/cell lab, the courier verifies the information mentioned on the transport documents in his/her possession and those provided by the CC (patient and donor codes, number and type of tubes provided, and also the data on the label of the HSCs bag) ;

The courier verifies information on the mandatory label placed by the collection center on the HSCs bag(s) to ensure its traceability;

The donor/collection center completes the information related to the collected product on their own form and also completes the Registry form CF/CI023 “collection/delivery report” and send them to the FGM registry by email. The CF/CI023 “collection/delivery report” form has to be dated and signed by both, the person who delivered the cells to the courier and the courier him/herself.

The graft is placed in the insulated container, at the temperature indicated by the cell therapy lab of the TC.

A pair of surgical gloves is placed in the container in case the customs require manual inspection of the graft;

Once the graft is placed in the insulated container, the container must be sealed by the cell therapy lab who delivers the cells to the courier, in order to secure it and to guarantee the cells' integrity; the seal number and the affix time are noted on the transport document;

The courier has to trace in writing (form CF/CI023 “collection/delivery report”) any unsealing of the container (at customs or before boarding) and, if this occurs, must reseal the container. He/she must consequently have replacement seals in his/her possession, provided by the cell therapy lab before departure (2nd seal number and affix hour also traced);

The courier delivers the HSCs without delay to the indicated address, handles it personally to the person designated by the TC's cell therapy lab, together with the collection report file and the CF/CI023 form “collection/delivery report”;

The courier requests the designated person at the cell therapy lab to fill in and sign the CF/CI023 form “collection/delivery report” and send it by email to the FGM registry coordinators, attesting the effective HSCs delivery to the TC and the completion of the mission.

4- Conservation of biological material of donors and recipients

The purpose of conservation of biological material is to allow the future use of cryopreserved biological material collected from unrelated donors registered and from donor/recipient pairs, for future research.

The stored samples can either be frozen cells, extracted DNA, or serum.

Samples can be requested using the prescription form.

The initial and final consent, both signed by donors, inform them that biological material will be stored for scientific purposes associated with the HSC donation performed.

It is recommended that a donor blood sample be taken the same day as the HSC collection to allow testings for infectious disease markers post collection..

The recipient's biological samples are collected at an optimal time, outside periods of aplasia, relapse, or conditioning.

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At least 2 cryo-tubes, containing each 5 x10^{6} viable cells, one from the donor and one from the recipient, are stored according to the applicable procedure in the concerned laboratories.

The material of the donor/recipient pair is stored according to the guidelines published in various study protocols (e.g., histocompatibility workshop).

A blood sample of at least 5 ml from the donor and from the recipient, is stored, in compliance with the legislation in force.

No biological sample of any kind can be stored by the TC if the donor, tested after reception of a blood sample, is not recruited or reserved for the patient.

5- Follow-up of patients who received an HSC allograft from an unrelated donor

Follow-up data for national patients who received a graft from an unrelated donor, regardless of the donor's registry of origin, are entered by the SFGM-TC into the EBMT Promise database.

The FGM registry may also forward basic information about the outcome of national transplanted patients, at the request of the international registry.

The follow-up of international patients is handled by their own registries.

6- Anonymity between donor and patient

In compliance with the legislation in force, unrelated HSCs donation is strictly anonymous.

"*The donor must not know the recipient's identity, nor can the recipient know that of the donor. No information enabling the simultaneous identification of the person who donated their body components or products and of the person who received them can be divulged." Article L. 1211-5 of the Public Health Code.*

Respect for anonymity extends in France to donors and patients, national and international, as well as to all facilities receiving donors and/or patients.

For international exchanges, the regulation of the strictest country must prevail.

7- Correspondence between donor and patient

Patients and donors may, if they wish, exchange correspondence, provided that anonymity is respected.

All correspondence received at the national DCs, TCS, or international registries (for any correspondence intended to French patients or donors) must transit to the FGM registry, which ensure that the principle of anonymity is respected. FGM translate the correspondence into English if necessary, and then transmit it to the concerned national DC, TC for the intended recipient.

No exchange of gifts, regardless of their value, or of photographs, is authorized

8- Financial aspects

A fee schedule detailing the terms of payment for additional tests, delivery of products, cancellations (linked to the main donor or back-up donor) and other services requested, is made available to the TCs by the ABM.

This fee schedule is sent annually, within a of 2 months pre-notice, to all TCs. If fees remain the same from one year to another, only the date changes on the fee schedule sent.

Any extra-cost of non-standardized requests is communicated to the requesting TC / international registry by email.

9- Record retention and archiving

Data relating to donors is stored in a totally secure manner in SYRENAD for the duration of their registration on the FGM registry, in accordance with the procedures and regulations in force.

The complete files are archived for 30 years in the case of allotransplants performed from donors hematopoietic stem cells [35], [36]

[35] Decision of the DG of the ANSM of February 7, 2020 defining the rules of good practice relating to the collection of tissues and cells of the human body from a living or deceased person, with a view to their therapeutic use

[36] Article R1112-7 of the Public Health Code

PATIENTS RECEIVING AN UNRELATED CORD BLOOD TRANSPLANTATION

1- Search for unrelated cord blood units

The search for an unrelated cord blood unit (CBU) starts with the patient's registration in SYRENAD. This request can only be made by a search unit associated with an authorized TC listed in the FGM registry database.

1.1 National Patients

1.1.1 Patients registration

The CF001 “registration form” is validated and co-signed by the transplant physician and the head of the HLA laboratory.
The administrative department of the TC issues a purchase order attesting its financial commitment to cover the following costs: patient’s registration on the national registry, search, and HSCs procurement, when available.

The indication of an HSC allograft is validated by a multidisciplinary committee, a mandatory procedure for all TCs in France (see decree DGOS/SDO/2005/101 dated February 22, 2005)

The patient's diagnosis must be one of those mentioned on the current list of indications, validated by the SFGM-TC and the EBMT. If the diagnosis is not on this list, the patient’s registration has to be reviewed and approved by one of the FGM physicians or by experts of the SFGM-TC, when appropriate.

The FGM coordination team verifies the completeness of the CF001 “registration form” upon reception and enter the data into SYRENAD, within the next 24 hours.

If the form is incomplete, the patient’s registration cannot not be processed and, the coordinators send a request for additional information to the TC search unit.

The information entered by the FGM coordination team is verified, corrected if necessary, and validated by the transplant search unit directly in SYRENAD, before the search process begins.

The patient's HLA typing, required at time of registration is, at a minimum, HLA-A*, -B*, -C*, DRB1*, and DQB1* intermediate level of resolution and DPB1 if available. HLA high resolution typing is strongly recommended to facilitate the search, and is mandatory before recruitment of a donor/CBU for transplantation.

1.1.2 Search for cord blood units

The list of international registries/CBB, where CBU search is possible, is available in SYRENAD.

Searches are automated in SYRENAD for the national and international registries connected to EMDIS-Cord and EMDIS: the search report is generated and sent automatically to the transplant search unit or international registry connected to EMDIS.

The exchanges with registries/CBBs not connected with EMDIS go through the FGM coordination team by email. These registries/CBBs send their search result.

Searches are repeated upon request..

1.1.3 Request for complementary tests

Complementary tests can be either, extended HLA typing, additional infectious disease markers, or requests for biological samples.

Requests for additional tests are sent by the transplant search unit:

- to national CBBs via SYRENAD and to EMDIS connected registries (automatic and secured process) ;
- via the FGM coordination team to non-connected international registries using the FGM specific form, by email.

The TC is notified of the date on which the samples were shipped:

- via SYRENAD, for a national CBU ;
- via SYRENAD/EMDIS, for an international CBU ;
- via email: for an international CBU belonging to a non-connected registry.

Samples of serum, plasma, or DNA of a national CBU can only be sent after reception of a formal shipment request of the CBU.

When the requested test is performed, the FGM coordination team send the results to the transplant search unit.

1.2 International patients

1.2.1 Registration and searches

EMDIS-Connected registries:

The patient registration is received via EMDIS. The international registry automatically get the search report.
International registries connected to EMDIS-CORD get a comprehensive data set on national CBUs in real time.
The international registry can decide to repeat the search. In this case, it receives, via EMDIS, the initial search report as well as any new information added.

Non-connected registries:

The international registry sends its own registration request form by email. The FGM coordination team register the patient into SYRENAD, run the search, print out the search report and send it to the international registry.
Searches are repeated on a one shot basis at each request of non-connected international registries.

1.2.2 Request for complementary tests

The TCs can request HLA complementary typings on selected CBUs.

Connected international registries:

The international registry sends its requests for complementary HLA typing or biological samples via EMDIS. They are received directly by the national cord blood bank via SYRENAD. The EFI accredited HLA laboratory, associated with the national cord blood bank, performs the requested tests or the CBB sends the requested samples, entering the corresponding information/result in SYRENAD.

If the tests are performed by the cord blood bank:

- The HLA typing results are entered into SYRENAD and the international registry receives them by EMDIS;
- The FGM coordination team send the results by email.

If an international TC performs itself the additional tests, FGM asks the TC to send the results by EMDIS, and the cord blood bank receives them directly in SYRENAD

Non-connected registries:

The international registry sends its requests to the FGM Coordination team, who enters them into SYRENAD, for direct transmission to the national CBB.
When biological samples are sent, the TC is notified by email of the shipping date, as entered in SYRENAD by the testing laboratory associated with CBB.

For testing performed by the national CBB, FGM coordination team sends the results, as entered by the bank into SYRENAD, to the international registry, by email.
If an international TC performs these tests, results have to be sent by email to the FGM coordination team, who enters them into SYRENAD for immediate transfer to the concerned CBB.

1.3 Reservation of a national CBU

1.3.1 Reservation following a request for HLA typing

The reception of a request for extended HLA typing automatically reserves the CBU until the results are entered-for a maximum period of 2 months. The status of the CBU in SYRENAD changes from Available (AV) to Temporarily Unavailable (TU).

The bank performs the requested HLA typing and enters the result into SYRENAD, which automatically generates a reservation for 2 additional months. The new status of the CBU changes from "TU" to "Reserved for this patient".
Beyond that period, the renewal of the reservation can only be granted after validation of the TC clinical arguments by the medical team of the FGM registry.

In all cases, and in the absence of an extension of the reservation or of a final selection, the CBU is released and made again available for any patient.

1.3.2 Reservation without a request for HLA typing

At the request of the TC or international registry FGM coordination team changes the status of a CBU from "available" to "reserved for this patient" for a2-months period.

At the end of this first reservation, and upon request, it can be extended for 1 more month.
Beyond that period, the renewal of the reservation can only be granted after validation of the TC clinical arguments by the medical team of the FGM registry.

In all cases, and in the absence of an extension of the reservation or of a final selection, the CBU is released and made again available for any patient.

2- Recruitment of CBUs

The coordination unit of the TC recruits the primary CBU selected. At this stage, the coordination unit ensures at least the existence and availability of a back-up CBU which can be recruited in parallel with the primary CBU to secure the transplant project.

2.1 Criteria of CBU / patient compatibility

The criteria for HLA compatibility is based on allele level for HLA-A, -B, and -C and DRB1 match.

- The SFGM-TC recommends:
- that the HLA-C locus be considered for the selection;[37]
- that TCs use CBUs matched for 8, 7, or even 6 of the 8 loci, while avoiding DRB1 mismatch whenever possible;
- a total nucleated cell (TNC) count > 3.10e7 /kg and CD34+ > 1x10e5/kg recipient's weight

2.2 Recruitment of a national CBU

The FGM registry coordinates the CBU shipment, in association with the concerned CBB and the TC or the international registry.

For a patient in France:
The TC coordination unit enters the data relating to the formal recruitment of the pre-selected CBU directly into SYRENAD.

Recruitment forms are generated from SYRENAD, then dated and signed by the transplant physician and sent by e-mail to FGM coordination team.
.
For an international patient:

The recruitment forms, duly signed and dated by the transplant physician, are sent by email to the FGM coordination team.

Upon reception, the final recruitment of the CBU is reviewed by an FGM physician and transmitted by email by the FGM coordination team within 24 hours to the corresponding CBB.

The CBB checks the integrity of the selected CBU bag, as well as the match between the CBU identification code and the code mentioned on the CBU bag.

Before shipment, quality control[38] and verification typing must be performed using a contiguous segment attached to the bag.[39]
This typing can be carried out by the CBB or by the requesting TC. The result must then be available at least 48 hours before CBU shipment.[40.]

The CBB, in association with the FGM coordination team, organizes the shipment of the CBU to the TC.

If the CBU is exported outside the European Union, the CBB requests an export authorization to the ANSM (with a copy to the FGM registry). The ANSM delivers the authorization only after receipt of the ABM Notice of Authorization.

[37] SFGM-TC 2012 workshop
[38] Form: CBUs characteristics according to RFSP
[39] Fact-Netcord standards (7th edition) E 3.2
[40] WMDA: Recommendation for use of CBU samples by CBBs and transplant centers (20180912_WGCB_Samples)

The lack of authorization is subject to prosecution.

This procedure does not apply within the European Union (EU) or with the European Economic Area (EEA).

2.3 Recruitment of an international CBU

The FGM coordination team organizes the shipment of a selected unit, working in close cooperation with the international registry/CBB and the TC.

The recruitment of an international CBU follows the procedure applied by each international bank/ registry. This procedure can vary from one country to another.

The TC enters the data related to the recruitment of the preselected/recruited CBU directly in SYRENAD.

The recruitment form is, then generated by SYRENAD, dated and signed by the transplant physician, and sent to the FGM coordination team by email.

Upon reception, the recruitment form is reviewed by an FGM registry physician and transmitted by the FGM coordination team within 24 hours via email, to the concerned international registry/cord blood bank.

Serum/plasma samples can be requested to complete any missing infectious disease markers.
All mandatory infectious disease markers must be tested, either by the TC or the cord blood bank of origin, and the results obtained before the CBU is shipped.

Before the CBU is released, quality control is required, as well as verification typing to confirm CBU identity. This verification typing must be performed using a contiguous segment attached to the CB bag.[41]
The international CBB can perform this typing, as can the TC requesting it. The result must be available at least 48 hours before the CBU is shipped.[42]

The international CBB organizes, in close collaboration with FGM coordination team, the CBU shipment to the French TC.

2.4 HLA typing at the time of release

The HLA verification typing is performed on a different sample than the one used for the first HLA typing performed at the time of listing the unit in the inventory.

If a discrepancy in the HLA typing appears, the FGM registry must be informed immediately. The international registry/TC can then decide to continue or to cancel the shipment request.

The FGM registry is responsible for the annual transmission of HLA discrepancy cases to the WMDA "HLA discrepancy" study group.

For the oldest banked CBUs, which may not have a contiguous segment attached to the bag, the CBB must have a procedure in place to verify the identity of the unit before shipment.

The FGM registry must inform the international registry/TC of the result before the CBU is shipped.[43]

[41] Fact-Netcord standards (7th edition) E 3.2.4
[42] WMDA: Recommendation for use of CBU samples by CBBs and transplant centers (20180912_WGCB_ Samples)
[43] Fact-Netcord Standards (7th edition) E 3.2

3- Importation of international cord blood units

International CBUs are shipped using a transport company selected by the international CBB and under its responsibility.

If the CBU is imported from outside the European Union, The cell therapy lab associated to the TC requests an import authorization from the ANSM (with a copy to the FGM registry). The ANSM delivers the authorization only after receipt of the ABM Notice of Authorization.

Importation without authorization is subject to prosecution.[44]

This procedure does not apply within the European Union (EU) ot with the European Economic Area (EEA).

Upon reception of the CBU, the TC's cell therapy lab must confirm the integrity of the bag.45

In case of any observed abnormality, the FGM registry must be immediately alerted, so that it can transmit the information to the international CBB or international registry. It is strongly recommended that any damage observed on the container (dry shipper) or on the bag/s be photographed.

The empty dry shipper must be immediately returned to the sending international CBB in its protective container.

4- Follow-up of patients transplanted with CBUs

A transplant physician's dedicated staff enters the follow-up data for French patients who received allografts from CBUs, regardless of the cord blood bank of origin, into the EBMT's "Promise'' database.

Additionally, the follow-up data for French patients who received allografts from national or international CBUs, and for international patients transplanted with CBUs coming from France or Europe, is analyzed within the Eurocord registry, located at the ABM.

5- Correspondence between the infant's family donor and patient

According to the recommendations established within the RFSP, no exchange of correspondence between the parents who have accepted the donation of their child's placental blood and the recipient is authorized.

6- Financial aspects

A fee schedule detailing the terms of payment for additional tests, delivery of products, cancellations (linked to the primary CBU or back-up CBU) and other services requested, is made available to the TCs by the ABM.

This fee schedule is sent annually, within a of 2 months pre-notice, to all TCs. If fees remain the same from one year to another, only the date changes on the fee schedule sent.

Any extra-cost of non-standardized requests is communicated to the requesting TC / international registry by email.

[44] Articles 511-8-2 of the Penal Code and L1272-8 of the Public Health Code
[45] Fact-Netcord Standards (7th edition) E 6.4.5

7- Record retention and archiving

The data of the mother and child are stored in a totally secure manner at the CBB for the entire period of CBU storage, in accordance with the procedures and regulations in force and are not made available for CBU searches, but only for inspection or assessment.

The complete files of mothers and children are archived for 30 years, in case of transplants performed with these CBUs. [46,47]

[46] Decision of the DG of the ANSM of February 7, 2020 defining the rules of good practice relating to the removal of tissues and cells of the human body from a living or deceased person, with a view to their therapeutic use

[47] Article R1112-7 of the Public Health Code