HÉMA-QUÉBEC

STEM CELL DONOR REGISTRY

Guide for Transplant Centres

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1. INTRODUCTION

1.1 What is the Guide for transplant centres?

The guide describes the processes surrounding:

- the search for compatible unrelated donors and cord blood units (CBU);
- the selection of donors and their preparation for donation;
- the purchase of cord blood units.

Its purpose is not to replace the internal policies and procedures of transplant centres (TCs), but to describe the minimum requirements that must be met in order to comply with the regulations and standards established by Health Canada and the World Marrow Donor Association (WMDA).

1.2 Application of standards and regulations

Each TC must be registered as an establishment with Health Canada and comply with the Safety of Human Cells, Tissues and Organs for Transplantation Regulations. For more information, consult the Health Canada Web site: **www.hc-sc.gc.ca**.

Under these Regulations, TCs are also required to comply with the Canadian Standards Association (CSA) standard sections referenced therein:

- cells, tissues and organs for transplantation: general requirements (Z900.1);
- lymphohematopoietic cells for transplantation (Z900.2.5).

For more information, consult the CSA Web site: **www.csagroup.org**.

Héma-Québec is accredited by the World Marrow Donor Association (WMDA), a non-profit organization created in 1994 that establishes international guidelines for the collection, distribution and transportation of hematopoietic stem cells. This organization provides access to more than 26 million donors and more than 650,000 cord blood units. For more information on the various international registries: **www.wmda.info**.

The information contained in this document is aimed at maximizing the quality of stem cell products prepared for recipients and the safety of stem cell donors all over the world.

As an organization accredited by the WMDA, Héma-Québec must ensure that the TCs and collection centres (CCs) under its supervision comply with the WMDA standards that apply to them. For more details on the WMDA: **www.wmda.info**.

TCs must follow industry best practices. They must also meet the standards of the Foundation for the Accreditation of Cellular Therapy (FACT), as agreed under the memorandum of understanding between Héma-Québec and the TCs. To consult FACT standards and requirements: **www.factwebsite.org**.

1.3 Training

The director of each TC is responsible for ensuring that all team members (coordinator, physician or support team members) involved in the transplant process (of stem cells from unrelated donors or cord blood units) are trained in accordance with this document.

2. THE STEM CELL DONOR REGISTRY

Héma-Québec is responsible for the Stem Cell Donor Registry, which includes a list of unrelated donors and the only Public Cord Blood Bank in Québec.

It provides stem cells in Canada and abroad. Its services include coordination of all the steps related to stem cell request, from the search to the transplant:

- donor recruitment;
- maintenance of the Québec computerized database;
- search for compatible unrelated donors and cord blood units for recipients in Québec or abroad;
- preparation of the selected donors for the donation;
- donor collection;
- banking and distribution of cord blood units;
- HLA typing (Human Leukocyte Antigen).

The Héma-Québec Stem Cell Donor Registry team is comprised of:

- a medical director;
- a department director;
- a department manager, search and distribution;
- case managers;
- medical secretaries;
- clerks;
- a scientific director.

A stem cell transplant may take place only when a donor's HLA typing corresponds to that of a recipient. The minimum typing requirements to proceed to transplant are: high-resolution HLA-A, HLA-B, HLA-C, HLA-DRβ1 for unrelated donors, and low-resolution HLA-A, HLA-B, and high-resolution HLA-DRβ1 for cord blood units.

The minimum compatibility required between a recipient and a donor is 7/8 at high-resolution for each loci HLA-A, HLA-B, HLA-C, HLA-DRβ1. For cord blood units, the minimum compatibility required is 4/6 at low-resolution for loci HLA-A, HLA-B and high-resolution for HLA-DRβ1.

Héma-Québec is a member of World Marrow Donor Association (WMDA), an international database in which Québec donors are listed under the code ION-6912. For more information on this organization, please visit: **www.wmda.info**.

3. CONFIDENTIALITY

3.1 General

It is very important that the TC protect the anonymity of the donor and the recipient in accordance with laws and regulations.

3.2 Identification of donors and recipients

When information is sent by email, donors and recipients must be identified solely by a number and their initials.

Records must be filed and stored under lock and key to prevent unauthorized staff from having access to them.

3.3 Information on the recipient and the donor during the search and the preparation for donation

No personal information on the donor (name, age, sex, location) is to be sent to the recipient or a member of the recipient's family.

Only information on the donor's health status may be sent to the TC by Héma-Québec if and only if this information helps determine eligibility and influences the final selection of the donor. In this case, the TC is responsible for informing the recipient of the donor's health status, in accordance with Health Canada's Safety of Human Cells, Tissues and Organs for Transplantation Regulations or the regulations applicable in their country.

3.4 Confidentiality during the transplant preparation process

It is important that TC staff involved in treating the recipient refrain from disclosing to the recipient information that can be used to locate or identify the donor.

Health professionals in Québec are therefore required to keep the following information confidential throughout the transplant and post-transplant process:

- the donor's country of origin;
- the donor's age and sex.

3.5 Confidentiality during transport

Only people who are directly involved in the collection or transport of the product may know the identity of the person transporting the stem cell product (courier). The courier must not have any contact with the donor, recipient or anyone who has a personal relationship with them. No document, gift or photo must be given to the courier to be exchanged between the donor and recipient.

It is up to the courier to ensure that no information appearing on the product or container compromises the donor's or recipient's confidentiality (name, country of origin, etc.), and that only the donor number appears on the product.

3.6 Correspondence and exchanges between the donor and the recipient

3.6.1 Anonymous correspondence between the recipient and the donor

After the transplant, anonymous exchanges between the donor and the recipient are allowed. The exchange of personal information is allowed only if there is mutual consent between the donor and the recipient, and the post-transplant waiting period specific to each registry is respected. For Québec, this period is one year following the donation. Some international registries do not allow exchanges between the recipient and the donor, regardless of Héma-Québec's policy.

The TC must ensure that no personal information (name, age, address) is included in any correspondence between the recipient and the donor, and it must forward this correspondence to Héma-Québec.

Héma-Québec ensures that no personal information is disclosed and verifies the content in order to maintain confidentiality. Gift exchanges are not allowed.

3.6.2 Request for exchange of personal information coming from a donor (Québec recipient)

It is recommended that the TC inform the recipient of the possibility that an information disclosure request might be made as soon as the donor begins to prepare for a donation. Héma-Québec asks that the TC respond as promptly as possible to avoid repeated requests from donors awaiting information.

At the donor's request, Héma-Québec informs the TC that the donor would like information on the recipient. In response to the donor's request:

- the TC must inform the recipient that the donor would like to exchange personal information and informs the recipient of the risks and restrictions involved in this exchange by providing the form ENR-01719;
- if the recipient agrees, he or she must complete and sign the form "Recipient's Consent to Release Personal Information to Donor" (ENR-02652) or "Consentement pour la divulgation d'information personnelle du receveur de cellules souches au donneur" (ENR-01719) and the TC must submit it to Héma-Québec;
- in the event of the recipient's death, a family member must complete the form "Consent to Release Recipient's Personal Information by Family Member" (ENR-02653) or "Consentement pour la divulgation d'information personnelle d'un receveur par un membre de sa famille" (ENR-01778) if that person wishes to correspond with the donor. The TC must send the signed document to Héma-Québec;

- ideally, the TC should notify Héma-Québec when the recipient or the recipient's family refuses to send any information;
- upon receipt of the signed consent form, Héma-Québec will send the recipient's personal information to the donor's registry.

Note: For international donors, the process will be handled by the responsible registry and forms equivalent to Héma-Québec forms are accepted.

3.6.3 Request for exchange of personal information coming from a recipient (Québec donor)

In response to the recipient's request:

- Héma-Québec will begin the procedure for obtaining the donor's consent;
- upon receipt of the consent form signed by the donor, Héma-Québec will send the donor's personal information to the TC or applicable registry.

4. COMPATIBLE DONOR SEARCH

4.1 Québec recipient

4.1.1 General

Héma-Québec performs all searches and prepares unrelated stem cell donors for donation for Québec recipients. This search is done using Héma-Québec's registry databases and international registries listed with the World Marrow Donor Association (WMDA).

A TC may request that Héma-Québec consult the WMDA to determine the probabilities of finding an unrelated potential donor before conducting an official search.

Searches for unrelated donors remain active at Héma-Québec until further notice from the TC. When two to three unrelated compatible donors are found, no additional analysis or verification typing (VT) will be requested.

4.1.2 Receipt of the search request

Upon receipt of the request and the required forms, Héma-Québec performs a search for potentially compatible cord blood units and donors.

Héma-Québec launches the search for any new request within one working day of its reception, if the HLA typing is complete.

4.1.3 Conducting a search

To perform a search for unrelated donors, the TC must complete and send to Héma-Québec the following documents:

- Form "Preliminary Search Request" (ENR-01560) or «Demande de recherche» (ENR-01564);

- A copy of the recipient's HLA analysis report or confirmation that samples have been shipped to the Héma-Québec laboratory for HLA analysis.

Important: The form "Preliminary Search Request" (ENR-01560) or «Demande de recherche» (ENR-01564) must be duly completed so that a search can be conducted, and it must contain the following information:

- recipient's first and last name;
- date of birth and sex;
- diagnosis and date of diagnosis;
- type of search: donor, cord blood or both;
- if mismatches are accepted, indicate which ones;
- recipient's weight (mandatory for cord blood unit searches);
- recipient's origin:
  - for example, Caucasian, Asian, Hispanic, etc.;
  - enter "other" if unknown;
- signature of the physician (or representative).

4.1.4 Search reruns

For difficult searches the Héma-Québec team will rerun the search every 90 days at a minimum to potentially identify compatible donors. The frequency of search reruns may vary according to the complexity of the recipient's profile and donor availability.

4.1.5 WMDA search request

Based on the availability of donors in the various registries, Héma-Québec asks the registry concerned to send it a detailed list of its donors. Héma-Québec uses this list to make its requests for additional testing (HLA-DRβ1, HLA-DQβ1, HLA-C, etc.) and its VT.

Note: The international registry may assign a number to the recipient. This number must be used in the steps that will follow (e.g., preparation for donation).

4.1.6 Search cancellation and reactivation

If the TC would like to cancel a search, it must complete the form "Search Cancellation" (ENR-01638) or «Fermeture de recherche» (ENR-01637) or its equivalent and send it to Héma-Québec.

To reactivate a search, the TC must send a new search request to Héma-Québec using form "Preliminary Search Request" (ENR-01560) or «Demande de recherche» (ENR-01564).

4.1.7 Verification typing

The search team requests VT for two or three donors (if possible) for each recipient, in accordance with the criteria established by the TC.

These requests require blood samples to be taken from the donor and analyzed in Héma-Québec laboratories.

Wherever possible, Héma-Québec forwards to the TC the following results:

- HLA typing performed in the Héma-Québec laboratory;
- virological markers from the donor's registry;
- virological markers from the Héma-Québec laboratory;
- information on the donor (blood type, history of blood transfusion, weight, travel, risk behaviours, etc.), if provided by the registry.

Héma-Québec keeps the donors selected for VT on reserve for 90 days (or in accordance with registry procedures) after the sample collection date. Following this period, the donor is no longer reserved. If the TC wants to keep this donor on reserve, it must make a request and provide a potential transplant date in the near future.

5. RECIPIENT TRANSFER

5.1 Change of transplant centre within Québec

When a recipient is transferred to another Québec TC, the TC accepting the transfer must complete the form "Patient Transfer" (ENR-01716) or "Transfert d'un patient" (ENR-01715). This form must be signed by both TCs involved and be forwarded to Héma-Québec, who will inform the various international registries involved in the search for this recipient.

5.2 Transfer of a Québec recipient to a transplant centre outside Québec

If the TC outside Québec requires information on a search already begun in Québec, it can contact its registry staff, who will approach Héma-Québec to begin the transfer of documents and results in complete confidentiality.

5.3 Transfer of a recipient from outside Québec to Québec

A TC that agrees to transfer a recipient from a registry outside Québec must submit the form"Preliminary Search Request" (ENR-01560) or «Demande de recherche» (ENR-01564) to Héma-Québec.

Note: The Québec TC must request that Héma-Québec approach the registry outside Québec to begin the transfer of documents and results of the previous search in complete confidentiality.

6. DONATION PREPARATION REQUEST

6.1 General

Once the VT is completed, the transplanting physician can select a donor for a donation preparation request.

All communications or correspondence between the TC and the CC must go through Héma-Québec. Exchanges between TCs and CCs may be authorized by Héma-Québec in exceptional cases.

Four to six weeks should be allowed from the time the donor is selected to the collection date.

Important: The TC must notify Héma-Québec as promptly as possible when the recipient's medical condition changes: deterioration of the condition, transplant cancellation, postponement of the transplant date, death or if the recipient is no longer eligible for a transplant. This is in the donor's best interest and prevents unnecessary pre-transplant evaluation, G-CSF injections or blood samples collections.

6.1.1 Policies of registries outside Québec

Policies regarding donor eligibility and availability criteria for a specific recipient may vary from one international registry to another (e.g., pathology, recipient's age, recipient's weight in relation to that of the donor, HLA compatibility, TC accreditation).

The international registry must provide Héma-Québec with proof that the CC and the analysis and manufacturing laboratories are certified or qualified in accordance with the regulations of its country (e.g., screening for infectious diseases).

Any request to prepare an international donor for donation is subject to the policies of the registry concerned.

Attention: If the registry accepts a maximum of two donations per donor, it will not be possible to request an additional donation from this donor. It is therefore important to be aware of the consequences that this requirement could have for a recipient if he or she were to require a second transplant or T- lymphocytes (DLI).

6.1.2 Collection centre qualification

Héma-Québec will provide the Québec TC with documents showing the CC qualification status, including procedures used and analyses conducted in compliance with Health Canada's requirements, by means of form "Qualification of an External Collection, Processing and/or Testing Facility" (ENR-01728) or its equivalent (e.g., Registry Statement). For some centres, this information can be obtained on the FACT or WMDA Web sites.

6.2 Urgent requests

In emergency situations, the TC may request that the VT and donation request be done simultaneously. It can take four to six weeks from the time the request is made to the time the report on the HLA results of the VT is produced. This timeframe may vary according to the availability of the donor and the CC.

Note: The TC must take into consideration the risk associated with the potential discovery of an HLA mismatch so that it can decide on the best plan of action.

When the process of preparing the patient for a donation is under way, it is important that the TC ensures that it has the human resources it needs to follow up with Héma-Québec within **one working day** concerning all questions or issues encountered.

6.3 Preparation of two donors simultaneously

Under exceptional circumstances, a TC may request that two donors be prepared for stem cell collection at the same time.

The preparation of two donors for donation simultaneously is subject to the policies of the registry responsible for each of the donors.

6.4 Request to prepare an unrelated donor for donation

The following forms must be completed by the TC (or their international equivalent) when an unrelated donor is selected for stem cell collection:

- "Workup Request" (ENR-02650) or «Requête de préparation au don de cellules souches» (ENR-02649);
- confirmation of donor typing;
- "Confirmation of Patient Typing" (ENR-02118) or "Confirmation du typage du patient" (ENR-02117):
  - if carried out outside the Héma-Québec HLA laboratory;
- donor and recipient HLA laboratory reports:
  - if carried out outside the Héma-Québec HLA laboratory.

6.4.1 Prescription and specifications

All requests, questions or specific requirements (e.g. quantity of cells, filtering, anticoagulant, etc.) must be specified on form "Workup Request" (ENR-02650) or «Requête de préparation au don de cellules souches» (ENR-02649) as soon as the request is filed.

Note: The sampling method, cell count, filtering, additive and anticoagulant vary from one CC to another. The TC must specify in its initial request whether it needs a specific dose and whether it has other requirements. The CC must then evaluate whether it can accommodate the TC.

6.4.2 Pre-donation samples

The TC has the option of requesting blood samples at the time of the donor evaluation. The acceptable volume for other registries is determined in accordance with their internal policies.

A maximum of 50 mL of blood can be taken from a Québec donor. Depending on the case, this volume may be increased for scientific research purposes.

6.4.3 Medical questionnaire

Donors selected for a stem cell collection must answer the medical questionnaire required by the registry in question. For Canadian recipients, Héma-Québec will provide a copy of the questions that donors were asked. All additional donor information not mentioned at the time of the VT is sent to the TC:

- preferences regarding the type of stem cell collection;
- donor availability;
- elements that can put the recipient in a high-risk situation, according to the applicable medical criteria; this information concerns:
  - travel to endemic areas where diseases such as malaria, Chagas disease, West Nile virus and Zika virus in particular are rampant;
  - risk behaviours and communicable diseases.

The TC must evaluate and confirm in writing that it accepts a donor with these risk factors in order to approve the start of the donation preparation process.

Note: The questionnaire may reveal a condition that could prevent the donor from making the donation.

6.4.4 Virological markers

At Donor evaluation

In Québec, analyses of virological markers, including West Nile virus, is conducted on all donors asked to prepare for a donation. For donors who answer “yes” to one of the three questions regarding Chagas disease, the Chagas test will be conducted on their blood samples as well.

Registries screen for infectious diseases in the 30 days prior to the stem cell collection, and the results are sent at the time of the final authorization for donation. However, the list of analyzed markers may vary according to the registry. Any additional analyses required which are not included in the donor’s evaluation must be requested when the workup is initiated.

Additional pre-donation sample analyses

If the TC requests that the CC also provide pre-donation blood samples to conduct additional infectious disease analyses in Héma-Québec’s laboratories, any abnormal results will be immediately shared between Héma-Québec and the TC.

7. WORKUP PLAN CONFIRMATION

If the donor cannot be available on the proposed dates for the donation, Héma-Québec will suggest alternative dates. The TC and the registry must confirm in writing that they agree to the dates proposed and confirm the start date of the recipient’s preparatory regimen.

Once the dates are confirmed, Héma-Québec will send the following information to the TC and the registry:

- the type of product that will be harvested (bone marrow or peripheral stem cells);
- the date of the medical examination, blood tests and virological marker analyses;
- the expected date of the final authorization for donation;
- the date and approximate time when the product will be available;
- the start date of G-CSF injections (if applicable);
- instructions for the courier;
- pre-collection sample details: company, shipment date and number (if applicable).

8. DETERMINATION OF DONOR ELIGIBILITY AND CLEARANCE

8.1 Donor eligibility evaluation

The donor's eligibility will be determined on the basis of the following:

- medical questionnaire;
- medical history;
- virological markers;
- risk behaviours;
- travel;
- physical examination.

It is the CC's responsibility to ensure that the donor is eligible according to applicable regulatory requirements. These requirements may vary according to the country in which the donor's registry is located, and it is the TC's responsibility to make additional requests in order to comply with both its internal policies and Health Canada regulations.

The transplanting physician is responsible for the final decision on whether to proceed with the transplant with this donor. This decision will be based on the donor's evaluation and eligibility documentation provided by Héma-Québec.

Note: It is the transplanting physician's responsibility to determine the need for an exceptional distribution and complete the associated documents, as required by Health Canada's Safety of Human Cells, Tissues and Organs for Transplantation Regulations and the Canadian Standards Association (CSA).

8.2 Donor final clearance

After receiving donor clearance to proceed with donation, the following forms or their equivalent will be sent to the TC/registry by Héma-Québec:

- "Donor Clearance" (ENR-01679) or "Autorisation au don" (ENR-01800).;

- "Verification of HPC, Marrow Prescription" (ENR-01690) or "Vérification de la prescription pour HPC, Marrow" (ENR-01796);
- "Verification of HPC, Apheresis Prescription" (ENR-01691) or "Vérification de la prescription de HPC, Apheresis" (ENR-01798) or "MNC, Apheresis DLI Prescription Verification" (ENR-01693) or "Vérification de la prescription / DLI par Aphérèse" (ENR-01797);
- results of virological testing less than 30 days prior to the donation;
- "Donor Health History" (ENR-01751) or "Histoire médicale du donneur» (ENR-01799);
- "Donor Medical Examination" (ENR-01768) or "Évaluation médicale du donneur" (ENR-01803);
- "Donor Medical Review" (ENR-01752) or « Révision médicale du donneur» (ENR-01804.

8.2.1 Prescription verification

Before proceeding with the recipient's preparatory regimen, the TC must have confirmed the specifications of the collection proposed by the CC, completed the appropriate section of the applicable form and sent it to Héma-Québec:

- "Verification of HPC, Marrow Prescription" (ENR-01690) or "Vérification de la prescription pour HPC, Marrow" (ENR-01796) or equivalent;
- "Verification of HPC, Apheresis Prescription" (ENR-01691) or "Vérification de la prescription de HPC, Apheresis" (ENR-01798) or equivalent;
- "MNC, Apheresis DLI Prescritpion Verification" (ENR-01693) or "Vérification de la prescription / DLI par Aphérèse" (ENR-01797) or equivalent.

Note: If the TC does not agree with the CC's specifications, they must reach a consensus prior to the recipient's preparatory regimen and prior to the donor's first G-CSF injection.

8.3 Ineligible donor

8.3.1 Donor risk factor

A cancellation or delay of the stem cell collection may occur if the examination or the results of blood tests prove to be abnormal. In some cases, the medical evaluation may reveal a potential risk for the donor, which requires additional investigation or exclusion.

8.3.2 Recipient risk factor

Before proceeding with a stem cell collection from a donor presenting a risk factor for a recipient, the TC must:

- evaluate the risks for the recipient;
- complete section 4 of "Donor Medical Review" (ENR-01752) or «Révision médicale du donneur» (ENR-01804) or the equivalent and send it to Héma-Québec.

Note: The decision to continue the process with a donor who poses a potential risk to the recipient (e.g. communicable diseases) is made by the TC based on an evaluation of the possible consequences. The TC must adhere to the

requirements for exceptional distribution as required by Health Canada or any other applicable regulations and obtain the recipient's consent.

9. PRODUCT TRANSPORTATION CRITERIA

9.1 General

It is the TC's responsibility to arrange for courier services and to plan and ensure that the stem cells collected for its recipient are transported safely.

The TC is responsible for training the courier.

The TC must ensure that the policies and procedures for transporting, shipping and receiving the product are in compliance with the applicable standards and regulations and are in keeping with WMDA recommendations.

Note: For all exceptional situations that could lead to a major issue while transporting the product, the TC may ask Héma-Québec for assistance in finding an alternative solution. The TC must notify Héma-Québec of any problem that might arise during product collection or transportation.

9.2 Courier selection

It is recommended that the courier be experienced in transporting stem cells in Canada before acting as a courier at an international level.

The courier must meet the following criteria:

- not be related to the recipient or the donor;
- have a passport which is valid for at least six months after planned travel date;
- be a self-reliant and resourceful traveller with experience in international transportation of stem cell products;
- be available until the product is delivered;
- have a credit card with a reasonable limit available;
- have access to a cellphone that can make and receive calls while roaming;
- have received training on the policies and procedures for the transportation of stem cells;
- have an acceptable knowledge of English or the language spoken in the country visited.

Note: Some registries or private companies (see 9.9) offer a stem cell transportation service. The TC is responsible for selecting the company based on compliance with the applicable standards.

9.3 Courier training

The TC is responsible for selecting, training and maintaining the skills of its couriers. The TC must have a courier training plan and maintain a training record based on applicable standards.

9.4 Courier's responsibilities

The couriers' primary responsibility is to ensure that harvested stem cells are transported safely and promptly between the CC and the TC in accordance with the TC's requirements (e.g., temperature). The other responsibilities are to:

- have on hand the documents regarding the product being transported;
- travel alone;
- keep the product on their person at all times (e.g., at their feet while in a restaurant or throughout the flight);
- not consume alcohol or products that could lead to impaired faculties;
- protect the confidentiality of the donor and the recipient;
- not accept gifts, letters or other items from the CC intended for the recipient;
- not purchase tobacco or alcohol outside the duty-free shop so as not to cause delays when going through customs;
- inform the TC of any delay;
- obtain the TC's instructions for issues related to a cell concentration that does not meet the TC requirements;
- verify the accuracy of the information on the product labels and samples accompanying the product (if applicable);
- package the product and check the product temperature in accordance with the protocol established by the TC;
- ensure that the product is not subjected to X-rays at airport security checkpoints or other;
- deliver the product directly to the TC at the location and to the person designated by the TC;
- verify the documents provided with the stem cell product.

9.5 Luggage

Airlines are introducing stricter rules with regard to the number, weight and size of suitcases. This includes the size of the stem cell product container. Despite using a minimum of personal belongings as carry-on baggage, the airline may request that this baggage be checked.

Note: The stem cell product container must never be checked for stowing in the baggage compartment, and it must never be placed with the personal belongings of the person transporting the product. In an airplane, the stem cell product must be placed beneath the seat in front of the person responsible for transporting the product and in their field of vision at all times.

9.6 Travel insurance and liability insurance

The TC must ensure that it has all the insurance necessary for the courier and the product itself to travel safely.

9.7 Air travel

The TC is responsible for making the necessary travel arrangements for the person transporting the stem cell product and ensuring compliance with the following:

- The return flight must have as few stopovers as possible;
- The courier must be seated in a location where he or she can evaluate the product temperature regularly during transport;
- A second flight (itinerary) should be planned in case of a major delay for the collection or a problem with the initial flight;
- The courier must reach the destination the day before the collection and must notify the CC of his or her arrival; if the courier wants to arrive the same day as the collection, the TC must notify Héma-Québec and obtain approval from the CC prior to departure;
- Any change to the initially planned transportation itinerary must be immediately communicated to Héma-Québec and to the CC, if applicable.

Here is a list of the information to provide:

- the flight number, if the ticket is already purchased, or book the reservation with the MEDA Desk agent;
- the person transporting the stem cell product must check in with a ticket agent directly at the counter.

The itinerary of the person transporting the stem cell product must be submitted to Héma-Québec and must include the following:

- the numbers and exact times of flights to and from the destination;
- the numbers and exact times of alternative flights to and from the destination.

9.8 Land travel

When the TC and the registry agree that it is more efficient to transport a stem cell product by land only (automobile, train or bus), the following rules apply in order to provide for unforeseen events (e.g. mechanical problems, accidents or other):

- two couriers must travel with the product so that one can drive the car while the other accompanies the product at all times, possibly deciding on another means of transportation if this should prove necessary;
- both couriers must hold a valid driver's licence;
- a GPS must be accessible;
- couriers must also have on hand a paper map of the route;
- couriers must have a cellphone with them;
- the courier must keep the box containing the stem cell product within reach at all times;

- alternative transportation methods must be planned in case of a major delay;
- any change to the original transportation itinerary must be immediately communicated to Héma-Québec and to the CC, if applicable;
- couriers are responsible for their driving and for any violations of the Highway Safety Code or any other pertinent law;
- the necessary automobile insurance must be obtained.

9.9 Commercial couriers

When a commercial courier is used, the TC must select a company that has a contract agreement with Héma-Québec (e.g., Cellex Medical Transports, Ontime Courier/ECS) which ensures compliance with WMDA standards, or a company that has been contracted by a WMDA-accredited registry for stem cell transport (e.g., NMDP).

10. TRANSPORT DOCUMENTS AND ITINERARY

10.1 Documents to be provided to Héma-Québec

The TC must have completed the following forms and sent them to Héma-Québec before the day of the donor's first G-CSF injection (if applicable) and at most four days prior to the courier's departure:

- "Stem Cell Product Transportation Details" (ENR-01701) or "Informations sur le transport de cellules souches" (ENR-01700) or its equivalent, and enclose a copy of the courier's itinerary.

10.2 Transport documents

Here is the list of documents that the courier must have on hand during transport:

- airplane, train and bus tickets;
- passport and visa, if applicable;
- confirmation of the hotel room reservation and travel insurance (arrangements by the TC);
- name, address and telephone number of a TC contact person available every day, 24 hours a day;
- delivery address provided on form "Workup Request" (ENR-02650) or «Requête de préparation au don de cellules souches» (ENR-02649);
- name, address and telephone number of a contact person at the CC available every day, 24 hours a day;
- cellphone number of Héma-Québec's on-call case manager (514-248-7908) and email address (hq-cases.managers@hema-Québec.qc.ca);
- letter from Héma-Québec (Héma-Québec will provide the TC with a letter to notify airport authorities) – the courier must have several copies of this letter on hand in order to provide a copy to all the authorities concerned: airport security, customs services and the CC and thereby avoid delays;

- the signed "Prescription Verification" form based on the type of product;
- the results of the donor's most recent virological marker analysis (within 30 days prior to the collection);
- import-export permits for stem cell transportation, as required by local authorities (Export permits can be provided by the international CC; import permits are not required in Canada.);
- collection report specifying the cell concentration;
- customs documents (provided by Héma-Québec and the CC);
- "Circular of Information for Cellular Therapy" (AABB/FACT or its equivalent);
- if applicable, a copy of the notification issued by Héma-Québec to the customs agency describing the courier's itinerary when entering Canada through Toronto, Montréal or Halifax;
- if applicable, a copy of the notification issued by Héma-Québec to airport security personnel and, if required, certain international airports (e.g., London Heathrow);
- the document associated with the exceptional distribution of stem cells explaining why they do not meet the usual criteria, if applicable;
- mandatory declaration forms, if applicable, in accordance with FACT standards.

11. SHIPPING BOX IDENTIFICATION

The product container must be clearly identified according to the TC's policy and contain the information required by FACT standards.

12. DAY BEFORE DONATION

Upon arrival in the city where the CC is located, the courier must contact the designated contact person and take the following steps:

- confirm his or her arrival at the destination;
- deliver the container and cooling packs, if requested by the TC or the CC;
- according to the TC's procedure, ensure that the cooling packs are refrigerated at 4°C or frozen at -20°C. Insulated coolers must be maintained at 4°C. Supplies and cooling devices may be stored in a refrigerator or a freezer accessible to the courier, in a properly identified bag. These arrangements must be made by the TC when the itinerary is prepared.
- confirm the product pick-up time and place;
- confirm the method of transportation between the CC and the airport or train station.

13. DAY OF THE DONATION

On the day of the donation, the courier must:

- be at the CC at the time and place agreed upon the day before;
- contact the designated person at the CC;
- have on hand the documents required to transport the product along with ID (passport, document with photo);
- check with the CC representative that the product is properly identified with the following information: the type of product, product type, number of bags, cell count, anticoagulant added, matches the stem cell prescription;
- package the product and samples accompanying the product according to the TC's instructions;
- verify all documents accompanying the product provided by the CC;
- declare the product on the customs forms, as required;
- supervise all inspections of the product at security checkpoints and at airport customs during transportation.

13.1 Product packaging

It is the TC's responsibility to provide the courier with the materials necessary to ensure that the product is transported safely in accordance with the TC's internal policies, with at least the following items:

- a rigid insulated container that is resistant to punctures, leaks, blows and changes in pressure;
- disposable gloves to be used if the product is inspected;
- a device that can measure the internal temperature of the container. It should be possible to take the reading outside the container.

The packaging and the container must ensure optimal temperature and conditions over a period long enough to cover any delays that might occur during transport.

The TC must not assume that the CC will provide the materials necessary for transportation. Any request by the CC for materials or devices must be approved and validated by Héma-Québec prior to the courier's departure. The courier must be familiar with the measures to take to maintain an adequate temperature.

Here are a few guidelines to consider:

- place the probe or thermometer on the top of the bag or between bags (if there are several of them);
- the product must not be in direct contact with the cooling agent, so that it does not freeze;
- gently agitate the container on a regular basis;

Note: All samples should be placed inside the shipping container after being inserted in a plastic bag and isolated from the product.

14. TRANSPORT AND DELIVERY OF THE STEM CELL PRODUCT

14.1 Product inspection at security checkpoints

If airport security insists on inspecting the product, it may be removed from the container for manual inspection under the courier's supervision. The shipping box itself can be inspected by X-ray.

If airport security requires an X-ray inspection of the product, and the product may not reach its destination within the required time without it, the courier may agree to an inspection of the product, but must request that the product not be stopped on the conveyor belt when it passes through the X-ray machine. The cumulative effect of X-rays on stem cell viability has not yet been determined.

14.2 Product delivery

Upon arrival in the city where the TC is located, the courier must:

- go immediately to the TC or the laboratory, according to the instructions set out by the TC;
- contact the designated contact person at the TC or the laboratory in order to deliver the product in person;
- enter the product temperature and arrival time at the TC;
- check the product and samples again with the information from the CC as well as the stem cell prescription;
- perform a visual inspection of the product to detect any irregularities (clot, tear, etc.);
- document and notify the TC of any event or incident that may have occurred during transport;
- obtain a signature confirming receipt of the product at the TC.

15. RECEIPT OF THE PRODUCT AND TRANSPLANT

The TC must confirm that the product was received in good condition and inform Héma-Québec of the transplant date using form "Product Delivery Record" (ENR-01729) or "Rapport de transport du produit" (ENR-01688) or its equivalent.

If the product is not administered to the recipient as planned, the TC must notify Héma-Québec immediately. The registry that provided the product may require the destruction of the stem cell product.

Note: The TC must immediately declare in writing to Héma-Québec any event related to the integrity of the product including any adverse reaction or event that may be associated with the administration of the product. Please refer to the section "Non-compliance and Reporting of AdverseReactions."

16. CRYOPRESERVATION REQUEST

To be able to cryopreserve an entire product, the TC must submit to Héma-Québec a request for cryopreservation using form "Stem cell product - cryopreservation request" (ENR-01704) or "Demande de cryopréservation du produit de

cellules souches" (ENR-01703) which must include the following information:

- the recipient's status, which explains the reason for the request;
- the reason for the transplant delay;
- the probability that the product will be transplanted;
- the new expected recipient preparation date.

Upon receiving this request, Héma-Québec notifies the registry so that it can obtain the donor's consent. The TC must obtain approval from the registry before the expected stem cell collection date.

If the request is approved, the TC must ensure that the product is:

- kept and used solely for the treatment of the recipient in the near future;
- kept and stored in a safe place in optimal conditions;
- destroyed if not used or is no longer viable;
- destroyed as soon as Héma-Québec notifies the TC that:
  - the donor does not consent to storage of the product or withdraws consent;
  - the donor or the registry requests that the product be destroyed.

The TC must inform Héma-Québec of the transplant date or if the product will not be administered to the recipient.

17. POSTPONING COLLECTION AND RESUMING PREPARATION FOR DONATION

17.1 Postponing collection

To postpone a collection date, the TC must advise Héma-Québec in writing of the specific reasons for this delay. The TC must propose a new timeline as soon as additional information and a new transplant date are known.

Héma-Québec notifies the registry and the CC of the change (postponement of collection or scheduling of a new date) and agrees on new dates according to their availability.

Note: Héma-Québec will notify the outside of Québec registry of any postponement in writing. The duration of the delay is subject to the policies of the concerned registry. Additional charges may apply.

17.2 Resuming the procedure for preparing for a donation

When the TC is ready to resume the stem cell collection procedure, it must notify Héma-Québec of the new transplant date, indicating whether new pre-donation samples are required. The registry could request that updated documents be submitted for the preparation for donation.

Note: Some registries may refuse to collect additional samples prior to the donation.

The donor's registry will take the following steps:

- determine whether the donor must undergo another medical examination;
- conduct a new analysis of virological markers;
- determine whether the donor needs to answer the medical questionnaire again.

Héma-Québec will send the final authorization for donation as well as the results of new virological analyses to the TC.

Note: Additional charges may apply.

18. CANCELLATION OF STEM CELL COLLECTION

To cancel a stem cell collection, the TC must send the reasons for the cancellation to Héma-Québec, in writing. . Héma-Québec will notify the registry only after it receives the written cancellation confirmation.

If the search for a potentially compatible donor is also cancelled, the TC must send to Héma-Québec form "Search Cancellation" (ENR-01638) or "Fermeture de recherche" (ENR-01637) or its equivalent.

Note: Charges may apply.

19. ADDITIONAL DONATION

19.1 General

Québec donors may only make two stem cell donations in their lifetime (not counting the DLI), and this includes one stem cell donation for a relative.

The criteria and policies regarding additional donations may vary from one registry to another. Héma-Québec will inform the TC of the various applicable policies.

At the time of the initial stem cell collection request, the TC must notify Héma-Québec if it anticipates that:

- the donor will be part of a research protocol;
- a second donation will be necessary.

The request will be analyzed by the registry's medical review team.

Note: A donor must be fully recovered before being approached for a second donation.

19.2 Application for an additional donation for the same donor or recipient

The following forms must be completed by the TC when requesting an additional donation:

- "Application for Additional Donation" (ENR-01697) or "Requête pour don supplémentaire" (ENR-03575) or its equivalent;
- all other documents that were required at the time of the initial application.

If necessary, the TC must answer any questions from the medical review committee or the registry's medical director in order to have the application approved.

20. CORD BLOOD UNIT REQUEST

20.1 General

At the TC's request, Héma-Québec:

- performs the cord blood unit search in Héma-Québec's Public Cord Blood Bank and the WMDA database;
- conducts additional analyses or the VT;
- coordinates the procurement of cord blood units for Québec's TCs.

Cord blood units are listed in the WMDA database. All correspondence between the TC and the cord blood bank or the registry must go through Héma-Québec.

Note: Cord blood units listed in the Héma-Québec bank appear in the WMDA database under the code ION-6912 (WO-1351).

When a cord blood unit is identified, Héma-Québec asks cord blood banks and registries to complete an additional form "Request for Additional Cord Blood Information (RACBI)" (ENR-02116) to show that:

- they are qualified for stem cell collection and treatment;
- they are certified and comply with regulations.

The transplanting physician is responsible for making the final selection of the cord blood unit. The TC is responsible for listing the requirements and completing the appropriate forms.

You will find information on cord blood bank certifications on the following Web site: **www.wmda.info.**

20.2 Cord blood unit search request

For Québec transplant centres:

Upon receiving form "Preliminary Search Request" (ENR-01560) or «Demande de recherche» (ENR-01564) or Héma-Québec will send to the TC the list of potentially compatible cord blood units listed in the WMDA database as well as the compatible unit summary from the Héma-Québec bank and other banks, as applicable.

For registries outside Québec:

Upon receiving form "Preliminary Search Request" (ENR-01560) or «Demande de recherche» (ENR-01564)or its equivalent, Héma-Québec will send the compatible unit summary from the Héma-Québec bank.

20.3 Request for a detailed cord blood unit report

If the WMDA search report reveals a cord blood unit that looks promising, the TC may obtain further details by requesting a report on the unit in question. Cord blood unit reports generally include basic information such as HLA typing, sex of the baby, cord blood collection date, CD34+ count, total nucleated cell count, viability and results of the mother's virological markers.

To obtain information that does not appear in the detailed report, the TC must submit a request in writing to Héma-Québec.

20.4 Request for extended HLA typing and verification typing

The TC may request that HLA typing be conducted by the cord blood bank itself or that the cord blood unit sample be shipped to the TC or to Héma-Québec for typing or other analyses.

20.4.1 HLA analysis conducted by the bank

To request extended or VT on a cord blood unit, the TC must complete the appropriate cord blood bank or registry forms, when required.

For a unit from Héma-Québec's Public cord blood bank, form "Cord blood unit request" (ENR-02188) or «Requête - Unité de sang de cordon» (ENR-02115) must be completed.

Note: Analysis times vary according to the cord blood bank. Banks generally do not conduct tests or VT if the results are already available in the report. The VT may also only be accessible following the reservation or purchase of the cord blood unit.

20.4.2 HLA analysis conducted by the transplant centre

Héma-Québec will ask the cord blood bank to provide details on the shipment of samples to the TC and will provide the TC with this information.

Note: Héma-Québec will inform the TC of the various cord blood bank and registry policies upon request. It is possible that the reservation or purchase of the cord blood unit may be required prior to the shipment of samples.

20.5 Other analysis requests

If a TC requires an analysis of virological markers, viability, CFUs or other for a particular cord blood unit, it must specify the desired analysis in writing and fill out the required forms.

For a unit from the Héma-Québec bank, form "Cord blood unit request" (ENR-02188) or «Requête - Unité de sang de cordon» (ENR-02115) must be completed.

Note: Analyses may be conducted by the cord blood bank in accordance with their policies and the availability of their samples.

20.6 Reservation request

To reserve a cord blood unit, the TC must forward a request to Héma-Québec specifying the desired reservation period. Héma-Québec will provide the TC with the forms to be completed, if required.

For a unit from Héma-Québec's Public Cord Blood Bank, form "Cord blood unit request" (ENR-02188) or «Requête - Unité de sang de cordon» (ENR-02115) must be completed.

Note: Reservation policies may differ according to the cord blood banks or registries. Most of them authorize reservations for two months at a time. An extension of this reservation period may be authorized when the TC specifies the reason for this extension along with a probable transplant date.

20.7 Purchase request

The TC must complete the purchase form for the cord blood bank concerned and specify the desired delivery date for the cord blood unit. The bank will confirm the possible dates and initiate the confirmation typing and other viability analyses.

For a unit from Héma-Québec's Public Cord Blood Bank, form "Cord blood unit request" (ENR-02188) or «Requête - Unité de sang de cordon» (ENR-02115) must be completed.

21. FILE CLOSURE (TRANSPLANT NOT RECEIVED BY RECIPIENT)

To close a search file, the TC must provide form "Search Cancellation" (ENR-01638) or "Fermeture de recherche" (ENR-01637) or its equivalent, which gives the reasons for the cancellation.

22. POST-TRANSPLANT FOLLOW-UP

22.1 General

Post-transplant follow-ups are necessary in order for the cord blood banks to be able to validate the effectiveness of their stem cell products, provide the WMDA with the required data and provide updates to the donor (if allowed).

Héma-Québec acts as the liaison between the TC, the donor and the registry outside Québec to coordinate anonymous exchanges between the donor and the recipient or the exchange of their personal information.

Note: Some registries do not allow information to be exchanged between the recipient and the donor. In this case, the exchange of personal information between a mother who donated her cord blood and a recipient will not be authorized.

22.2 Recipient health status update

To obtain a recipient health status update (100-day and annual post-transplant follow-ups) or a death notice, Héma-Québec

asks the TC to complete form “Post-Transplant Follow-up” (ENR-02004) or “Suivi post-greffe” (ENR-02005) or or its equivalent.

Note: Additional requests regarding the recipient’s health status by the donor will be submitted to the TC by Héma-Québec. Recipients or their families must have consented in writing to the disclosure of information on their health status to Héma-Québec, to the donor and to the registry outside Québec.

23. NON-COMPLIANCE AND REPORTING OF ADVERSE REACTIONS

23.1 General

Héma-Québec defines non-compliance as any deviation from a requirement. This non-compliance must be immediately communicated in writing to Héma-Québec.

For any non-compliance occurring at the TC, the latter is responsible for declaring the event to Héma-Québec, conducting a cause analysis, detecting the problem, implementing corrective measures at its centre and notifying Héma-Québec.

The TC must inform Héma-Québec of any adverse reaction occurring in the recipient that might be associated with the product and notify Health Canada of errors, deficiencies and side effects associated with the transplant, in accordance with regulations. Form “Serious Event Reporting” (ENR-00114) or “Déclaration d’évènement grave” (ENR-00113) or its equivalent, describing a transfusion reaction, must be submitted to Héma-Québec as promptly as possible.

Héma-Québec must report to the WMDA any event considered serious or any adverse reaction to the stem cell product (“Serious Product Events and Adverse Reactions (SPEAR)” or “Serious Events and Adverse Reactions (SEAR)”). Declaration criteria include but are not limited to the following (for the recipient or the stem cell product):

- death;
- illness;
- unexpected hospitalization or considerable prolongation of hospitalization;
- a persistent or major disability;
- thawed cord blood unit;
- leak in the stem cell product.

24. COSTS AND BILLING FOR QUÉBEC TRANSPLANT CENTRES

24.1 General

The costs of conducting searches for and obtaining stem cell products from an unrelated donor are described in this section.

Please note that for registries outside Québec, costs change about once a year and may vary from one registry or cord blood bank to another.

For the list of current prices for the various registries, please contact Héma-Québec’s Registry Manager.

24.2 Costs related to the search for a compatible donor and cord blood unit

All expenses related to the search and identification of donors or cord blood units are covered by Héma-Québec (e.g., high-resolution HLA-DRB1, VT request, transportation and sample collection). Expenses related to preparation for donation and for product transportation are the responsibility of the TC.

24.2.1 Costs for a Québec donor

- No invoice is sent to the TC by Héma-Québec.
- There should be direct billing between the CC and TC (as defined by the Ministère de la Santé et des Services Sociaux).

24.2.2 Costs for a Canadian donor (excluding Québec)

- **Evaluation and collection costs:** The Canadian CC bills the Canadian TC directly. These costs may vary from one CC to another. It is also possible for a CC to bill Héma-Québec directly; this amount will then be charged back to the TC.
- **Donor expenses:** The Canadian Registry One Match will bill Héma-Québec for donor expenses. The TC will then be charged back for donor expenses associated with preparation for donation and the donation itself.
- **Costs for postponement or cancellation of stem cell collection:** The TC can be billed for blood sampling, donor evaluation and any other donor expense, as applicable.
- **Transportation:** The TC is responsible for expenses incurred for transporting the product from the CC to the TC.

24.2.3 Costs for an international donor

- **Evaluation and sampling costs:** Héma-Québec receives and pays the invoice sent by an international registry. An invoice in the same amount is then sent to the TC.
- **Costs for postponement or cancellation of stem cell collection:** Costs related to the cancellation or postponement of a stem cell donation for which Héma-Québec receives an invoice will be billed to the TC.
- **Transportation:** The TC is responsible for expenses incurred for transporting the product from the CC to the TC.

24.2.4 Costs for a cord blood unit

- **Product:** Héma-Québec receives and pays the invoice from a bank or registry.
  - For Québec recipients covered by the Québec Health Insurance Plan (RAMQ), the product is charged back directly to the Ministère de la Santé et des Services sociaux du Québec.
  - For recipients from outside Québec (not covered by the Québec Health Insurance Plan) who have received a transplant in Québec, an invoice is sent to the TC.
- **Transportation:** Héma-Québec receives and pays the invoice from a registry outside Québec. An invoice in the same amount is then sent to the TC.

Original text in French. In the event of a discrepancy between the English and French versions, the latter will prevail.