MANUAL
COLLECTION CENTERS

Brazilian Registry of Voluntary Bone Marrow Donors (REDOME)
Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA)
MINISTRY OF HEALTH

SUMMARY

Presentation

Created in 1993, REDOME (Registry of Voluntary Bone Marrow Donors) has consolidated its position as the third largest registry of voluntary bone marrow donors in the world and this success must be shared with the entire network that has worked to ensure access to potential donors and patients to the registry throughout the Brazilian territory.

However, maintaining a nationwide registry in a country the size of Brazil is a major challenge, especially in the subsequent location of this donor and in the steps that involve complementary tests for identification and confirmation of compatibility, fundamental to the success of hematopoietic progenitor cell (HPC) transplantation, highlighting, in this scenario, the work of blood centers and histocompatibility laboratories.

The displacement of selected donors to specialized collection centers and the assurance of a humanized and safe environment in the evaluation of these donors is also a result of REDOME's work with the various professionals who receive them.

Throughout its history, REDOME has endeavored to keep up with the technical and scientific changes that have promoted a significant improvement in transplant results for patients who find in the voluntary donors of our registry, the renewal of their hopes for a full and healthy life.

Guided by values such as ethics, transparency, cooperation and innovation, we thank the successful partnership with blood centers, histocompatibility laboratories, transplant and collection centers and present in this document some general guidelines that seek to strengthen this activity for the benefit of our donors and patients.

Dr. Danielli Oliveira

REDOME’s Technical Coordinator

Introduction

REDOME has prepared this manual with the purpose of offering information and guidance on the best practices in the stages of medical evaluation, laboratory tests, collection of hematopoietic progenitor cells (HPC) for transplantation, transportation of biological products, and follow-up of voluntary donors after collection.

The processes involve an important flow of information exchange and compliance with standards determined by current regulatory standards and international recommendations, always aiming at the safety of donors, patients and all the professionals involved.

1. Guidelines

1.1. Privaciy and Data Protection

REDOME acts to ensure the privacy of all users of its computerized systems, patients and donors, and advises that all information provided during the identification process of a compatible donor for allogeneic transplantation, respects the privacy of patients and donors, according to REDOME's Privacy Policy and in accordance with the General Law of Data Protection.

All employees involved in this activity should be informed about their responsibility in this process and the collection center should act, together with REDOME, to ensure privacy and protection of donor data.

All documentation sent to REDOME must use the donor's identification code (DMR or GRID) and the donor's initials (when indicated) in order to maintain the anonymity of the donation.

Under no circumstances, the approach to the voluntary donor by a professional of the patient's care team should be allowed, in order to ensure the exemption of the evaluation and the donor's autonomy.

In the event the donor performs the evaluation at the same center as the patient, a different team, independent from the patient (preferably from the hemotherapy service) must perform this evaluation and all professionals involved must act to ensure the donor's privacy.

The collection center must make the results of complementary exams performed to the donor available upon request.

1.2. Donor Autonomy

In the first appointment at the collection center, the donor should receive all the explanations about the workup stage, including the clinical and laboratory tests performed, and about the collection procedure, highlighting the voluntary nature of the donation.

The consent form for the collection of HPC must be applied by a professional involved with this activity, experienced in the evaluation of voluntary donors for collection. This consent form must be signed before the conclusion of this stage.

The donor should be oriented about the different sources of stem cells for collection and the possibility of participating in the choice of the source to be collected.

Depending on the donor's wishes or the indication for transplantation, only one source may be appropriate. In this case, the donor should be oriented about the indication indicated by the patient's transplant center, remaining free to express his desire and make the decision about it.

The donor must be informed about the risks related to the donation and also about the risks for the patient, from the moment the conditioning starts, in order to emphasize that any reluctance or withdrawal must be expressed before this step.

1.3. Collection Center Autonomy

REDOME recognizes and reinforces the autonomy of the collection center in the process of evaluation and collection of volunteer donors, but understands that donor safety and transplant success depends on good communication between the collection center and REDOME's team in order to identify additional risks and unexpected events and act to reduce possible damage to all involved.

In case of donor inability identified during the work up process, due to clinical condition or laboratory test results, the donor should be informed by the professional at the collection center who performed the care in order to clarify doubts and provide guidance on specialized medical evaluation, if indicated.

REDOME must be informed about the results of tests performed in the voluntary donor during the work up, including altered results that justify not clearing the donor, but the collection center must not inform the transplant center about the cause of the donor's unsuitability.

2. Pre-collection Clinical and Laboratory Evaluation (Work-up)

The donor should be informed by the collection center about the tests that will be performed during the work up, in compliance with the legislation in force, and as described in the forms provided by REDOME.

If it is impossible to perform an exam or if it is necessary to perform exams that are not foreseen, REDOME must be informed in order to evaluate alternatives to the test in question.

2.1 Clinical Evaluation

The donor clinical evaluation consists of the donor health questionnaire and donor health history, as described in the corresponding forms[1] (FOR009 Donor Final Evaluation and FOR004 Donor Final Clearance).

[1] Forms cited in this Manual will be made available by REDOME, as requested.

The questions are not restricted to those presented on the form, and the physician must ask questions in order to assess problems that may compromise the health of the donor and the recipient.

REDOME highlights the following aspects:

- Family history of hemoglobinopathies, which may indicate the need for hemoglobin electrophoresis;
- Donor coming from a malaria endemic area - should be questioned about the history of infections and have a specific exam to rule out active infection in a reference laboratory. In case of infection by P. malarie (quartan fever) the donor will be considered unfit;
- Donor with a history of psychiatric disease - evaluate the medications being used and the donor's current emotional state, especially considering the impact of the experience and stress related to donation. The list of conditions;
- Donor with a previous or current history of lower back pain - bone marrow HSC collection is contraindicated in this case;
- Donor with a history of conditions associated with chronic pain - assess the risk of worsening pain conditions due to the procedures associated with donation and inform the donor;
- Donor with a history of tattooing, piercing, or equivalent procedure in the last 12 months - the transplant center should evaluate the additional associated risk and consider the benefit of the transplant and the availability of other donor.

2.2. Laboratory Tests

The laboratory tests that must be performed in the work up stage are:

- Complete Blood Count;
- INR/ Prothrombin activation time;
- APTT;
- Blood typing: ABO and Rh factor and Irregular Antibodies Research (IAR);
- Beta HCG - for female donors of reproductive age. This test must be repeated up to 7 days before the collection;
- Urea
- Creatinine;
- Gamma GT;
- Alkaline phosphatase;
- GOT;
- GPT;
- Total Bilirubin and fractions;
- Glucose;
- Total Proteins and Fractions;
- Amylase;
- Lipase.

The infectious disease markers (serologies) considered mandatory are described below:

- HBs Ag;
- Anti-HBc (IgG or IgG+IgM);
- Anti-HCV;
- Anti-HIV 1 and 2;
- NAT HCV;
- NAT HBV;
- NAT HIV;

- Anti-HTLV I/II;
- Syphilis (VDRL or FTA-ABS);
- Anti-CMV (IgM and IgG);
- Anti-EBV (IgM and IgG);
- Anti-Toxoplasmosis (IgM and IgG);
- Chagas Disease Serology.

The following tests are also recommended:

- Malaria (test for plasmodium or plasmodium antigens) for donors living in endemic regions, with active transmission, or coming from these regions less than 12 months ago;
- Anti HSV1-2 (IgM and IgG);
- Hemoglobin electrophoresis - mandatory in case of hereditary hemoglobinopathy in the family;
- Protein Electrophoresis.

2.3. Other Tests

Depending on the source of cells selected and risk factors associated with the donor or institutional protocol, the collection center may also perform other complementary tests:

- Chest Radiography (Posterior-anterior and lateral);
- Electrocardiogram.

2.4. Donors Unsuitablility

The exams listed in this document, as well as the eligibility criteria, are those foreseen in the legislation in force.

Donors who present the following conditions should be considered unsuitable:

I. Reagent/positive test for HIV-1 or HIV-2 virus;
II. Reagent/positive test for HTLV-I or HTLV-II virus;
III. Non-reactive HBsAg test with reactive anti-HBc, except when the Donor is anti-HBs reagent;
IV. Reactive HBsAg test and/or positive NAT test for the HBV virus; in the case of CPH for unrelated conventional transplantation purposes, this condition applies, except when the Recipient also has a reagent HBsAg test and/or positive NAT test;
V. Reactive anti-HCV test and/or positive NAT test for the HCV virus; in case of HPC for the purpose of unrelated conventional transplantation, this condition applies, except when the Recipient also has a reactive anti-HCV test and/or positive NAT test;
VI. Reactive test for Trypanosoma cruzi;
VII. Malignant neoplastic disease, except basal cell carcinoma of the skin and carcinoma "in situ" of the cervix;
VIII. Medical condition that places the Donor's health at risk;
IX. Condition observed in the clinical, social and laboratorial screening that may result in serious risk to the health of the Recipient;
X. Causes of temporary inability to donate blood, according to specific legislation in effect;
XI. Pregnancy in progress or puerperal women (up to the 6^{th} month).

A listing of conditions and medications most frequently associated with donor unsuitability is available in the Appendix and additional information is available on the World Marrow Donor Association (WMDA) website under Donor Medical Suitability

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

Other complementary exams or specialist evaluation may be requested at the collection center's discretion.

3. About Hematopoietic Stem Cell Sources

3.1. Apheresis Donation

In the collection of HSC by peripheral blood apheresis, the following requirements must be fulfilled:

a) The collection center must make a contact telephone number available to donors for any questions or complications.

b) The collection procedure must be supervised by an experienced medical professional available to act in case of complications.

c) The administration of granulocyte growth factor (G-CSF or Filgrastim) must follow the standard dose established in the literature and be supervised by a professional experienced in the administration and complications related to the use of these drugs.

d) It is not recommended that the donor stay away from the collection center during the period of use of the growth factor, but in selected cases, and according to the collection center's evaluation, the donor can take the administration at home.

e) The donor should be informed about the possibility of a second collection day.

f) In case of severe complications associated with the apheresis procedure, the collection should be interrupted immediately and REDOME should be informed.

g) The collection center should not release the donor or interrupt the procedure without the knowledge of the transplant center and REDOME.

h) The donor can be released on the same day of the collection if there is no medical contraindication. However, this donor should stay close to the collection center for at least 24 hours.

i) REDOME recommends that the donor has a blood sample collected for complete blood count and platelet and electrolyte count before returning home.

j) In case of mobilization failure, compromising the collection of HSC, REDOME must be informed immediately and the possibility of a new collection, after the use of Plerixafor (according to the protocol provided by the collection center) or bone marrow collection must be evaluated. The donor must be informed and consulted about the final decision.

3.1.1. Central venous catheter implantation

In cases where a central venous catheter must be implanted to perform apheresis collection, REDOME recommends that this procedure be performed only in cases where there is no other option. The other criteria are:

a) The center must have a protocol for peripheral venous access evaluation and central venous catheter placement.
b) The possibility of replacing the peripheral blood source with bone marrow should be considered and the donor should be consulted about this possibility.
c) The placement of a central venous catheter should only occur after peripheral access has been evaluated. This evaluation should be done by an experienced professional and documented on the donor's final evaluation form.

d) REDOME recommends the use of femoral central venous access, avoiding access to the internal jugular or subclavian vein.

e) The donor must be informed about the venous access to be used and about a forecast of the number of collections. In case of change in the schedule of the number of collections, the donor should be promptly informed.

f) Before placing a central venous catheter, the donor must sign a specific consent form (Term 06) for the venous access that will be used and the risks of this procedure.

g) After the implantation of the central venous catheter, the donor should remain hospitalized until its removal.

3.2. Donation Via Bone Marrow Puncture

The following requirements must be fulfilled for the collection of HPC via bone marrow puncture:

a) The collection center must evaluate the need for collection of an autologous blood unit, considering the patient's and donor's weigh.

b) REDOME recommends that in case of autologous blood collection, the unit should be obtained from a hemotherapy service up to 15 days before the date scheduled for the HSC collection. In case the unit is not used, the donor must be informed about its disposal.

c) REDOME does not recommend the use of granulocyte growth factor (G-CSF or Filgrastim) for bone marrow collection. Exceptional cases should be evaluated together with the REDOME team.

d) The donor should be informed about the type of anesthesia used and its potential risks as well as the position adopted for the puncture of the iliac crest and potential complications such as lower back pain and functional disability, for example.

e) The donor should not be released on the same day of the collection, remaining hospitalized for 24 hours. REDOME recommends that the donor has a blood sample collected for complete blood count and platelet and electrolyte count before being released.

f) At hospital release, the donor should receive orientation regarding rest, the use of analgesic medications, and the need for ferrous sulfate replacement for anemia treatment.

g) A medical certificate, provided by a medical professional of the collection team, should guarantee the days of leave required for full recovery. REDOME recommends 7 days leave, but this period may be reviewed by the collection center.

4. Documentation[2]

The adequate filling out of the forms and terms is a fundamental step for the safety of the donation process.

REDOME recommends that the collection center sends the requested forms (in the current version indicated), duly filled out and without erasures, and ratifying the compliance with the required dates.

The work up procedure starts when the prescription for the transplant is forwarded by the transplant center.

The national prescriptions are sent on form FOR027 - Prescription for HSC collection and the international ones can be sent on form FOR011 - Prescription for stem cell collection or on the requesting registry's own model.

[2] Forms and terms cited in this Manual will be made available by REDOME, as requested.

After conference and approval by the search technical team, REDOME will forward to the collection center the transplant center's prescription.

At this stage, it is essential to evaluate the possibility of attending the donor on the dates indicated or alternatives offered by the REDOME team. The collection planning must take into account the dates of the exams, results, mobilization/hospitalization, and expected collection.

In addition to the prescription, documents will be sent for completion during the work up process and subsequent return to REDOME.

4.1 Work Up for National Patient

- **FOR042 – Tests and Collection Schedule** - document with the donor's orientation regarding the day of the exams and collection, address of the collection center, preparation, contact people. The document also guides the donor about the preparation for the collection procedure and hospitalization (if any), with dates and time;
- **FOR035 – Work up plan -** should be completed with the donor collection schedule and the patient infusion and conditioning dates;
- **FOR009 – Final donor evaluation -** should be filled out with the results of the tests performed during the work up. This document must also inform risk factors or conditions that require the attention and approval of the transplant center (e.g. donor with a history of tattooing less than 12 months ago, donor with risky sexual behavior, etc.);

- **Term02 – Term of Consent for Work Up and Collection -** should be applied, explained and signed by the donor on the date of the medical consultation. The document must be sent to REDOME after the first work up appointment;
- **Term06 – Term of Consent for the use of Central Venous Catheter -** when there is the need for the use of a central venous catheter. The document must be sent to REDOME before the collection;
- **Term 07 - Term of Consent for Cryopreservation** - when there is the intention to cryopreservation of the product for later infusion**.**

The document must be sent to REDOME before the collection.

4.2. Collection for National Patient

The collection process begins after the Transplant Center's acceptance in **FOR009 - Donor Final Evaluation**. After that, REDOME will send, along with the Transplant Center's acceptance, the following documents:

- **FOR029 - Transport Report -** should be used whenever the collected product is sent to another center;
- **FOR030 – Quantification report -** must be filled out right after the donor's collection; informing the source and the quantity of cells of the collected product. The document must be sent to REDOME as soon as possible;
- **FOR043 - Post-collection report -** must be filled out with information about the collection procedure and the donor's conditions post-collection and at discharge. The document must be sent to REDOME as soon as possible.

4.3. Work Up for International Patients

- **FOR036 - Donor Health Examination Request (work up) -** document generated by REDOME that informs the collection center of the donor's personal data;
- **FOR037 – Work Up Plan -** document in which the collection center indicates the planned dates for the work up and collection. This document must be sent to REDOME for later submission to the international registry, which, in turn, will indicate the planned dates for patient conditioning, transplantation, and whether the product will be infused fresh or cryopreserved. The purpose of this document is to ensure that the centers work in line with the planned dates, avoiding delays or cancellations. The document must be filled out at the beginning of the process, as soon as the dates are set;
- **FOR008 – *Courier Instructions* -** document with the Courier's guidelines, such as place and time to pick up the product, contact name and phone numbers, lodging suggestion. This document must be filled out at the beginning of the process, as well as the Work up Plan, and returned to REDOME;
- **FOR042 – Tests and Collection Schedule -** document that provides guidance to the donor regarding the date of the exams and collection, such as the address of the collection center, preparation, and contact persons. The document also guides the donor about the preparation for the procedure and hospitalization (if any), dates and times;
- **FOR004 – *Donor Final Clearance*** – document that will record the donor's evaluation and the results of laboratory tests and should be sent to REDOME, at the end of the work up, within the timeframe established in the Work up Plan, for later submission to the international registry;

- **FORM-F70 – *Verification*** – document that has the objective of confirming the receipt and understanding of the medical prescription by the service responsible for the collection;
- **Term 02 – Consent Term for Work Up and Collection-** should be applied, explained, and signed by the donor on the date of the medical appointment. The document must be sent to REDOME along with FOR004 and FORM-F70-Verification**;**
- **Term 06 – Central Venous Catheter Consent Form** – when there is the need to use a central venous catheter. The document must be sent to REDOME before the collection;
- **Term 07 - Consent Term for Cryopreservation** – when the product is expected to be cryopreserved for later infusion.

4.4. Collection for International Recipient

The collection process begins after the Transplant Center's acceptance in **FOR004 - Donor Final Clearance**. After that, REDOME will send, along with the transplant center's acceptance, the following document:

- **FORMC010 – Collection Report –** the original form should be delivered to the Courier and a copy should be sent to REDOME by e-mail;
- **FOR010 – Transport Report** – should be filled out by the collection center and courier upon delivery and conference of the product. This document must be sent with the material and a copy sent to REDOME;
- **FOR043 – Post-collection Report** – should be filled out and forwarded to REDOME for donor health monitoring purposes.

5. Subsequent Donation

Subsequent donation is defined by the donation of HPCs made by a donor registered in REDOME who has already donated HPCs.

Requests for subsequent donations should follow the usual procedure for a prescription, respecting the deadline and the number of donations allowed.

During the evaluation process for subsequent donation, the donor's autonomy to donate a second time, as well as the privacy and confidentiality of personal data, must be guaranteed.

At the moment the new prescription is sent by the transplant center to REDOME, the donor's conditions for donation will be verified.

In case a new donation is needed, the minimum interval between them should be 45 days, but the request can be sent by the transplant center 30 days after the first collection, along with a technical justification for the new donation.

REDOME's medical team will evaluate the new request considering the collection procedure performed initially and the donor's clinical condition during the 30-day follow-up evaluation.

The exchange of the cell source is recommended in the case of bone marrow collection, but in the case of peripheral blood donation, a second collection from the same source is possible.

Apheresis HPC collections that occur in more than one session qualify as a single donation.

5.1. Lymphocyte Donation

Lymphocyte donation is not considered a subsequent donation.

The use of granulocyte growth factor (G-CSF or Filgrastim) is not indicated for lymphocyte collection.

6. Guidelines for Labeling and Releasing of HPC

The labeling, completion of documentation, and proper release of Hematopoietic Progenitor Cells (HPC) is extremely important for the transport and maintenance of the integrity of the collected material in order to ensure the safety of the patient for whom it is intended.

6.1. Labeling

The material must be prepared and labeled in accordance with current regulatory standards, accreditation body requirements, including the WMDA.

The labels of released products must be tamper evident and remain intact throughout the storage period, until the expiration date of the product, and contain the following information:

- Total cell volume;
- DMR or GRID ID;
- Receiving RMR;
- Expiration date and time 48h;
- Date and time of collection;
- Volume of anticoagulant;
- Temperature at 2-24ºC;
- Do not irradiate;
- Do not use leukocyte filter.

The other information about the product must be described in the collection form that must accompany the product (**FOR029 - Transport Report or C10 - Collection Report**)**.**

6.2. Sample Labeling

The samples to be sent should be identified with the donor's identification number in REDOME (DMR) and date of collection, for national destination.

In case of international sending, the label sent by REDOME must be used.

6.3. Courier

The person responsible for transporting the material is trained to meet the requirements established in national and international standards.

It is important to point out that the couriers for international collections are foreigners, and it is important that the person responsible for receiving the material is able to receive and communicate with this professional.

If a second collection day is required or if there is any incident that delays the release of the product, REDOME must be informed immediately

In case of international courier, he/she will inform the transplant center his/her country of origin that will take the appropriate measures related to logistic adjustments.

The courier should check, upon pick up, the product identification according to the label and the identification described in the request. In case of discrepancy of information, document the non-compliance found and inform REDOME. The transport conditions should be registered by the courier, if cooled or at room temperature, date and time of transport and additional comments.

6.4. Documentation for Sending Cells[3]

All released products must accompany the following documentation:

- **FOR029 – Transportation Report** (National);
- **FOR030 – HPC Quantification Report** (National);
- **FORMC010 – Collection Report** (for export);
- **FOR010 – Transport Report** (for export).

6.4.1. FOR029- Transportation Report

The transportation report aims to register the preparation and verification of the material for transportation.

The Release Information field must be completed by the collection center, with the information of RMR (recipient ID), DMR (donor ID), and donor initials. The product information, such as product type (bone marrow, apheresis, or DLI), number of bags shipped, total nucleated cells, volume, collection date, number of tubes, date and time of release.

Upon receipt of the product for transport, the courier must complete the field Courier Verification of Material. The purpose of this field is to register the double check of the material prepared for transport, indicating if the information matches the Release Information field.

[3] Forms cited in this Manual will be made available by REDOME, as requested.

The transplant center, upon receipt of the product, must document the date and time of receipt of the material and verify the conditions of temperature, number of bags and tubes listed.

After being completely filled out (collection center and transplant center), this form must be sent to REDOME.

6.4.2. FORM030 - HPC Quantification Report

This document must be filled out by the collection center with the pertinent information.

In the General Information field, indicate the Source of Cells (bone marrow, peripheral blood, or lymphocytes), DMR (donor's identification code in REDOME), RMR (recipient's identification code in REDOME), Quantity of cells requested (dose per kilogram of the recipient), donor's weight, recipient's weight, ABO/Rh typing of the donor, ABO/Rh typing of the recipient, the respective ABO/Rh incompatibility if any, and whether the product has been handled.

In the case of bone marrow collection, the following must be informed in the corresponding fields: date of collection, date and time of shipment, total volume of the bag, volume of anticoagulant, quantity of cells collected (CNT/Kg of recipient) and quantity of total cells (CNT).

In the case of peripheral blood collection, the following information must be documented: date of each apheresis session, respective bag volumes, respective CD34+ doses, and date of shipment. In the case of a second collection, the document must be completed again with each shipment.

The Lymphocytes (CD3+) field must be filled out only in the case of collection of this material, with the following information: date of collection, volume of bags, dose of CD3+ by weight of the recipient, and date and shipping of the product.

Complementary Information must include the anticoagulant used, the handling of the product, and whether there were any complications before or after the collection of the cells.

In case of a serious adverse event with the donor or the product, REDOME must be immediately notified.

6.4.3. FORMC010 – Collection Report

For HPC collections for international shipment, in substitution of FOR030, the FORMC010 - Collection Report must be filled out.

This form must be filled out with the type of product collected - Marrow (bone marrow), HPC Apheresis (HPC from peripheral blood), MNC (mononuclear cells), DLI (lymphocytes).

In the PATIENT DATA field you must document information such as Patient ID - Assigned by donor registry (RMR).

In the DONOR DATA field the Donor registry = REDOME, Donor ID (DMR), Date of birth, Gender - Month - Day), Gender, Weight, CMV, Blood group/RhD (ABO/Rh).

In COLLECTION CENTER, the following must be informed: Institution, Address (address of the collection center), ZIP Code, City, Country, Attention (contact person at the collection center), Phone, Fax, and e-mail.

In PRODUCT DATA, the following information about the collected product must be registered: Collected volume in mL, Anticoagulant volume in mL, Donor plasma volume in mL - applicable, other additives, please specify, Totals in mL, Total number of nucleated cells in 10ˆ8, CD Pos in % (select cell type and percentage), CD Pos in 10ˆ8 (select cell type in 10ˆ8, CD pos in 10ˆ6 patient weight in kg (select cell type in dose per kilogram of the recipient), hematocrit in % (percentage of hematocrit). The information should be filled in by day of collection and the total for each field viewed at the bottom of the table in the Totals column.

On page 2, under PRODUCT DATA (continued), indicate the Amount of whole blood processed in mL, Overnight Storage (if applicable) per bag and its storage temperature (temperature stored) and number of hours (number of hours). It should also be recorded whether CD34 enumeration was performed (Is CD34 enumeration performed?) and transport temperature (Transport Temperature).

In STEM CELL COLLECTION DATA, information must be recorded for each collection day, if applicable. The fields to be completed are: Collection Date of stem cell collection - year, month and day, Time started (start time - with time zone), Time completed (end time - with time zone), Tissue culture media used (when applicable), anticoagulant used (anti-coagulant used).

In the field ADDITIONAL SAMPLES ACCOMPANY STEM CELL PRODUCT, inform Sample Type and the volume in mL in the respective type of tube used (heparin, EDTA, ACD, anticoagulant or other).

6.4.4. FOR010 – Transport Report

The international transport report is intended to record the preparation of the material and the verification on delivery for transport.

Initially, donor identification in Donor ID (DMR), donor GRID number (international donor ID), Patient ID (RMR), and recipient initials (Patient Initials) should be documented in the IDENTIFICATION field.

The Release Information field must be filled out by the collection center with the product information - type of product, bone marrow (HPC, Marrow), Apheresis (HPC Apheresis), or lymphocytes (DLI); number of bags sent, total nucleated cells, volume, date of collection, number of tubes, date and time of release (date of product release).

Upon receipt of the product for transportation, the courier must complete the fields under Courier Verification and Packaging Information in the FOR010 - Transport Report. The purpose of this field is to register the double check of the material prepared for transport, indicating if the information is adequate with the description in the Release Information field.

The transplant center, upon receipt of the product, must document the date and time of receipt of the material, the temperature conditions, the number of bags and tubes.

When the registration of the information is completed, the form must be sent to REDOME, by the transplant center.

7. Adverse Events Related to the Donor or the Product

Serious events and adverse reactions, either donor- or product-related, can occur and be identified at different points in the HPC donation process.

The main sources of adverse event information are collection reports (forms), transportation reports, post-collection (follow up) evaluation records, transplant center notifications, and international records.

The collection center is responsible for identifying and analyzing the adverse event involving the donor and/or the product in the collection-related steps and must notify REDOME and the applicable health authorities

REDOME, in turn, must identify the occurrences involving the donor, the collected product or the recipient, and identify the need for adverse event registration and investigation.

7.1. Adverse Events Qualification Criteria

Events classified as a serious event or adverse reaction, related to the product, the donor or the patient, must include one of the following criteria:

- Serious adverse event or reaction, classified as serious and unexpected, occurring to the donor or to the patient;
- Fatal or life-threatening event for the patient or donor;
- Any undesirable occurrence associated with the transportation, processing, storage, and distribution of cells intended for transplantation that could lead to disease transmission, death or life-threatening, disabling, or conditions that could result in, or prolong, patient hospitalization or morbidity;
- Event related to the use of medication that affects the health of the donor or patient;

- Product with lower cell count, bacterial contamination, or laboratory error leading to clinical complications for the patient.

7.2. Adverse Event Reporting

The collection center must use the FOR024 - SEAR Registration and FOR025 - SPEAR Registration forms[4] to notify the REDOME about serious adverse events involving the donor (SEAR) or the product (SPEAR)

Once an event classified as Adverse Event (SEAR or SPEAR) is identified, forms containing the relevant information must be sent to the REDOME analyst responsible for the collection, so that an investigation and assessment of the event can be started.

The work up team, upon receiving the Adverse Event record, should immediately inform the supervision of the responsible area and the REDOME coordination for evaluation of the actions to be taken and the respective case follow-up.

The collection center must notify Anvisa of the adverse reaction using a standardized form, called "Adverse Reaction Notification Form", available at https://pesquisa.anvisa.gov.br/index.php/241757?lang=pt-BR and the form has fields that correspond to the minimum information necessary for the investigation and evaluation of the case.

7.2.1. Reporting to WMDA (World Marrow Donor Association)

[4] Forms cited in this Manual will be made available by REDOME, as requested.

As a WMDA member, REDOME is committed to notifying the international organization about the occurrence of adverse events for international registration purposes.

According to the WMDA classification, adverse events can be classified as:

- **Adverse reaction to a donor** during or after the donation procedure or negative occurrences including unnecessary procedures;
- **Adverse reaction in a recipient** during infusion of a cellular product, including damage due to product quality, delayed delivery, etc;
- **Risk of Harm -** Is the occurrence of any problem or incident, but without negative consequences to the donor, recipient and/or system.

The reporting to WMDA should be done, by REDOME, using the information provided by the collection center through the indicated forms and the questionnaires sent by e-mail.

8. Post-collection Donor Follow-up

The follow-up of voluntary donors after the collection of HPC consists of evaluating their physical and emotional well-being, and attending to any eventual occurrences.

After hospital release, REDOME recommends that the collection center informs donors about possible adverse events and makes a contact channel available for any questions. Within 30 days post-collection, the donor should return to the collection center, whenever possible, for clinical re-evaluation and a new blood count.

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Another strategy in the follow-up of donors undergoing HPC collection is performed by a REDOME team professional (doctor, nurse, or other health care professional, properly qualified and trained) at 7 days, 30 days, and 1 year after collection, preferably by telephone.

The effectiveness of this approach depends on the receipt of the collection information contained in the FOR-043 Post-Collection Report of Hematopoietic Cells from Unrelated Donors - REDOME. In this regard, this form should be sent to REDOME as soon as possible.

In the first year after the collection, in the identification of events or adverse reactions possibly associated with the donation of HPC, a re-evaluation of the collection center may be requested

After the first year of donation, the donor will be followed for a period of 10 years, through an electronic questionnaire and the selected cases will also be submitted to evaluation by telephone contact.

In case of reevaluation by the collection center, REDOME will be responsible for the donor's travel expenses to the new evaluation.

9. Confidentiality of Donor and Recipient Data

Voluntary donation of unrelated hematopoietic progenitor cells is anonymous.

The confidentiality of personal data aims to protect the donor and recipient from unwanted contact of any nature, avoiding pressures on the donor and recipient, such as financial and emotional blackmail.

In order to preserve the privacy of donors and patients, REDOME presents the following guidelines:

- During the work up and collection, the donor can be informed about the origin (national or international) of the patient;
- Donor and patient should be informed not to share on social networks any information that could identify them (e.g. day and place of the donation or transplant);
- After the collection**,** REDOME contacts the donor to inform the infusion date, in case of cryopreservation.

9.1. Post-transplant Communication

After six months from the date of the infusion, the donor may request information about the recipient's health status, and eighteen months after the transplant, a break of confidentiality between donor and recipient is authorized.

In the period of six to eighteen months, correspondence exchange is allowed (without data that allow the identification of the donor or recipient), but REDOME does not allow the exchange of gifts.

The anonymity breaking and disclosure process is a voluntary process that will be evaluated and conducted by REDOME. It must be approved by both donor and recipient and, in the case of the recipient, it will still be necessary for an evaluation from the responsible medical team authorizing the meeting.

Whenever desirable and respecting the rules and deadlines described above, the collection center may encourage its recipient/donor to write us through the e-mail postransplante@inca.gov.br with the purpose of initiating disclosure, exchange of letters and news among their peers.

10. Final Remarks

Some descriptions of the proper handling and filling of documents in the HPC request process were presented.

These guidelines do not dispense the clarification of doubts by the REDOME team for the correct use of requests and forms.

Contact the REDOME team through:

Email: rereme@inca.gov.br

Telephone: (21) 3207 - 4707

Website: http://redome.inca.gov.br/

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Attachment - Listing of Valuation Conditions and Removal from hematopoietic progenitor cell donation

Listing of Valuation Conditions and Removal from hematopoietic progenitor cell donation	
DISEASES	
CONDITIONS	**STATUS**
Aneurysm	Removed
Chronic Alcoholism	Removed
Angina (feeling of tightness, pressure, heaviness or pain in the chest)	Removed
Sickle cell anemia	Removed (Sickle Cell Trait - Released)
Arrhythmia	Released - must be evaluated by the collection center
Psoriatic Arthritis	Removed – Autoimmune
Rheumatoid Arthritis	Removed – Autoimmune
Septic Arthritis	Assessment
Arthritis	Released
Asthma	Continuous oral corticosteroid use - **Temporarily removed for 3 months.** Using inhalation pump - **Released**
Cerebrovascular accident	Removed
Babesiosis	Removed
Systemic Blastomycosis	Removed
Cancer - Carcinoma	For all types of Cancer - **Removed**, except skin and cervix - see below
Skin Cancer	Basal Cell Carcinoma of the Skin Treated with Surgery Only - **Released** Basal Cell Carcinoma of the Skin Treated with Medication or Radiation Therapy - **Removed** Melanoma - **Removed**
Cervical Cancer	Treated with surgery only - **Released** Treated with chemotherapy or radiotherapy - **Removed**
Cirrhosis of the liver	Removed
Anaphylactic Shock (Anaphylaxis)	Removed
Conjunctivitis	Released
COVID 19 (infected individuals with clinical and/or laboratory diagnosis)	Suspected Covid-19 and mild infected - **Keep active in the system and do not collect a sample until 10 days after the onset of symptoms.** Infected with moderate/severe symptoms requiring hospitalization - **Medical Evaluation.**

COVID 19 (individuals who had contact with persons with a confirmed diagnosis for COVID)	**Keep active in the system and only collect a sample 10 days after contact and/or onset of symptoms.**
Uveitis (iritis, iridocyclitis, chorioretinitis); scleritis; (episcleritis)	Released - collection center evaluation
Chemical Dependency	Evaluation
Diabetes	Released. Only keep the donor off insulin.
Dermatitis	Released - collection center evaluation
Spondylometaphyseal dysplasia	Evaluation
Celiac disease	No Medication Use - Released
Chagas disease	Removed
Addison's disease	Removed
(Adrenal insufficiency)	Removed – Autoimmune
Crohn's disease	Evaluation
Psychiatric Disease	Depression - Cleared Schizophrenia - Withdrawn Panic Disorder - Evaluation Bipolar Disorder - Withdrawn Other illnesses - Evaluation
Parkinson's Disease	Removed
Von Willebrand's Disease	Removed
Wilson's Disease	Evaluation
Renal Disease	Transplanted - Withdrawn Dialysis - Withdrawn Single kidney - Released - evaluation by the collection center
COPD (Chronic Obstructive Lung Disease)	Removed
Elephantiasis (filariasis)	Removed
Pulmonary Embolism	Removed
Pulmonary Emphysema	Removed
Endometriosis with controlled pain and no signs of anemia	Released
Epilepsy	On medication - Removed No medication for more than 3 years and no crisis - Released
Scoliosis without surgery and impediments in	Released
daily life	Removed
Multiple Sclerosis	Removed
Amyotrophic Lateral Sclerosis	Removed – Autoimmune
Ankylosing Spondylitis	Removed
Yellow Fever	Evaluation
Rheumatic Fever	Evaluation
Fibromyalgia	Removed
Pheochromocytoma	Removed
Monoclonal Gammopathy	Removed
Glaucoma	Released

Low White Blood Count (Leukopenia or low WBC)	Evaluation
Gout	Released
Leprosy	Removed
Hemochromatosis	Released
Hemophilia A and B	Removed
Intracranial Hemorrhage (hemorrhagic stroke)	Removed
Herniated Disk	Evaluation
Herpes	Labial or genital, no active lesion or treatment - Released Labial or genital lesion, under treatment - Removed for 30 days Herpes zoster - Removed for 6 months
Hepatitis A	Released
Hepatitis B	Removed. In case of Hepatitis B with positive antiHBc and negative viral load, it may be evaluated by Collection Center
Hepatitis C	Removed
Hypertension	Released
Hyperthyroidism	Removed
Hypothyroidism	Released
HIV	Removed Donor with HIV+ partner should also be Withdrawn even with negative test.
HTLV	Removed
Acute Myocardial Infarction	Removed
Heart Failure	Removed
Adrenal insufficiency	Removed
Spinal cord injury - spinal cord injury with paraplegia or quadriplegia	Removed
Lupus	Removed – AI
Malaria	With a history of quartan fever (Plasmodium malarie) - Removed. For other forms (P. vivax and P. falciparum) - Released
Myasthenia Gravis	Removed
Neurofibromatosis	Removed
Osteopenia	Released
Osteoporosis	Released
Chronic pancreatitis	Removed
Pemphigus Foliaceus	Removed – Autoimmune
Thrombocytopenia	Evaluation
Psoriasis	With use of topical medication (ointment, cream or gel) - Released. Using oral medication - Removed.
Purpura	Removed
Sexually Transmitted Disease	Evaluation
ulcerative rectocolitis	Removed
Rheumatism	Evaluation

	History of rheumatism in childhood treated and cured - Released
Sarcoma	Removed
Sarcoidosis	Removed
Syphilis	Treated and cured - Released Under treatment - Removed for 12 month
Cushing's syndrome	Removed
Guillain - Barré syndrome	Removed
Marfan syndrome	Removed
Raynaud's syndrome	Removed
Sjogren's syndrome	Removed
Antiphospholipid antibody syndrome (APS)	Removed
Genetic syndromes (Edwards, Klinefelter, Down's syndrome)	Removed
Tourette's syndrome	Removed
Heart murmur	No use of medication and need for medical follow-up - Released. Other forms require evaluation.
Beta thalassemia minor or thalassemia trait	Genetic Feature - Released
Beta Thalassemia (major and intermediate)	Removed
Immune Thyroiditis (e.g. Hashimoto's thyroiditis)	Released
Sickle cell trait	Released
Toxoplasmosis	Treated for more than 6 months - Released In Treatment - Evaluation
Thrombophilias	Removed
Thrombosis	Removed
Pulmonary Tuberculosis	Treated for more than 5 years - Released
Extrapulmonary Tuberculosis	Removed
Leydig's Tumor	Removed
Cardiac / cerebral valve	Removed
Vitiligo	No Medication Use - Released
Drugs	
Acitretin (teratogens - for psoriasis and other skin diseases)	Removed for 3 years after discontinuation of medication
Platelet Antiaggregant –(E.g: clopidogrel, persantin, ticlid, and ASA	Released
Antibiotic – E.g: azithromycin, vancomycin, clavulin, meropenem, amoxacillin, neomycin, polymyxin B, benzetacil, penicillin, erythromycin, gentamicin, cephalexin, amikacin, oxacillin	Released
Oral antifungals - fluconazole, tolmicol, amicozol	Released
Topical antifungals	Released

Anticoagulants – E.g: Heparin, warfarin, Xarelto	Removed for 6 months
Antiallergic E.g: Allegra, fenergan	Released
Antipyretics and analgesics - Dipyrone , Paracetamol (Tylenol)	Released
Antivirals – E.g: acyclovir, zovirax, tamiflu	Evaluation
Opioid analgesics – E.g: morphine, methadone, fentanyl	Evaluation
Anti-inflammatory drugs – E.g: ibuprofen, nimesulide, ketoprofen, alginac, toragesic	Released
Antihypertensive (for Hypertension) – E.g: nifedipine, monochordil, adalat, isordil, sustrate	Released
Antidepressant – E.g: fluoxetine, sertraline, amitripyline, citalopram	Released
Antiparkinsonian – E.g: biperidene, prolopa, azilect	Removed
Antipsychotic - haldol, quetiapine, clozapine, iloperidone, lurasidone, olanzapine, quetiapine, risperidone and ziprasidone)	Removed
Anxiolytic – E.g: espran, alprazolan, bromazepan, lexotan, valium and sleeping pills	Released
Antacids – E.g: antak, sonrisal, cimetidine	Released
Contraceptive	Released
Arrhythmia	Evaluation
Bronchodilators – E.g: aerolin, aminophylline, theophylline, atrovent, berotec	Released
Vitamin K	Evaluation
Tranquilizer - E.g: diazepam, valium, lorax, lexotan, thiopental, neozine	Released
Constipation – E.g of laxatives: mineral oil, lactulone, dulcolax, milk of magnesia	Released
Convulsion (Anticonvulsants – E.g: phenytoin, gardenal, phenobarbital**)**	**With history of seizure - Removed** **When used for migraine - Released**
Oral Corticoid	Evaluation (Detail reason for use, dosage)
Topical Corticoid (ointment, cream and gel)	Released
Inhaled Corticoid (for asthma)	Released
Nasal decongestants	Released
Dutasteride (teratogenic - used for benign prostatic hyperplasia)	Removed for 180 days after discontinuation of medication
Expectorants - Ex: fluimucil, carbocysteine, bromelin	Released
Danazol (hormone for the treatment of endometriosis and fibrocystic breast disease)	Evaluation
Gastric discomfort – E.g: omeprazole, pantoprazole, ranitidine	Released

Diabetes – E.g: galvus, glifage, glibenclamide, metformin	Released. Remove donors on insulin
Diarrhea – E.g: imosec, floratil	Released
Diuretics – E.g: hydrochlorothiazide, furosemide	Released
Etretionate (teratogenic - used for severe psoriasis)	Removed
Finasteride (teratogenic - used for baldness and benign prostatic hyperplasia and CA of prostate)	Removed for 30 days after discontinuation of medication
Hormones	Evaluation
Female Hormones for the treatment of menopause	Released
Female Hormones for Cancer Treatment Cancer	Removed
Isotretinoin (teratogenic - used for severe acne)	Removed for 30 days after discontinuation of medication
Appetite Moderators	Released
Nausea and vomiting – E.g: plasil, nausedron, dramin, bromopride, vonau	Released
Sedatives – E.g: midazolam, propofol, dormonid	Released
Colesterol Treatment –E.g: simvastatin, atorvastatin	Released
Testosterone	Removed for 6 months after suspension of medication
Use of injectable anabolic steroids without prescription	Removed for 12 months from the date of last use
Vaccines	Released
Allergy Vaccin	Released
Verminosis – E.g: metronidazole, albendazole, mebendazole	Released
Other conditions	
Angioplasty	Removed
Accident with sharp-edged material contaminated by organic fluids (e.g. blood)	Removed for 30 days
Breastfeeding	Child exclusively breastfed (less than 6 months) – Removed Child older than 6 months - Released. The breastfeeding suspension period will depend on the source of the cells to be collected Postpartum - Removed for 6 months regardless of delivery and whether she is breastfeeding.
Cardiac Surgery	Removed
Bariatric Surgery	Removed for 6 months
Lung Surgery (total or partial removal)	Removed
Spleen surgery (total or partial removal)	**Removed** By trauma/accident - Released after 12 months
Cataract or myopia surgery	Released after discharge by ophthalmologist
Surgery to remove the appendix	Released after 3 months

Hemorrhoid removal surgery	Released after 3 months
Hernia correction surgery	Released after 3 months
Varicose vein removal surgery	Removed for 3 months
Plastic surgery	With local anesthesia - Removed for 3 months With general or epidural anesthesia - Removed for 6 months
Tonsillectomy surgery	Removed for 3 months
Gallbladder removal surgery	Removed for 6 months
Uterus removal surgery	Removed for 6 months
Backbone surgery	Removed for 6 months
Thyroid removal surgery	Benign disease - Removed for 6 months If thyroid cancer - Removed
Breast lump removal surgery	Benign Nodule - Removed for 6 months Malignant nodule - Removed
Orthopedic surgery	Removed for 6 months
Polytrauma surgery (multiple lesions, injuries usually caused by accidents)	Removed for 12 months
Surgery for partial or total removal of the partial or total removal of the large intestine	Removed for 12 months For bowel cancer - Removed
Kidney removal surgery	**Removed for 12 months** **For kidney cancer - Removed**
Treatment of varicose veins with sclerotherapy (medication injected directly into the varicose veins)	Removed for 7 days
Platelet donation by apheresis	Removed for 2 weeks
Chronic back pain that is severe and has impact on daily life	Removed
Mild and occasional back pain related to exertion (including sciatica) and with occasional use of medication	Released
Back pain from fracture or dislocation	Released
Pregnancy	Removed for 6 months after childbirth
Hypermenorrhea (excessive menstruation) or other menstrual disorders	Released
Pacemaker	Removed
Endoscopic procedures (endoscopy and colonoscopy)	Removed for 6 months
Weight < 50Kg	Released for BM donation - consider compatibility with patient's weight Evaluation PB donation - apheresis parameters
Obesity -	BMI > 40 - Removed BMI 30-40 - Evaluate other risk factors
Piercing, tattooing, permanent makeup	Released
Prostitution	Removed

Dental treatment (including root canal, abscess drainage, extraction, caries, with or without anesthesia) or without anesthesia)	Released
Renal stone treatment with extracorporeal lithotripsy	Removed for a month after the procedure
Previous transfusions	Removed for 12 months after the last transfusion
Transplanted (for all organ types including cornea)	Removed
Orthomolecular Treatment	Released
Marijuana	Released
Cocaine	Inhalation - Removed for 12 months from the date of last use Injectable - Permanently removed
Crack	Removed for 12 months from the date of last use
Other Drugs	Evaluation

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