INCA
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MANUAL
HISTOCOMPATIBILITY LABORATORIES

REDOME
INSTITUTO NACIONAL DE CÂNCER

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 represents 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 stem cell 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

The objective of this Manual is to guide histocompatibility laboratories on how to perform the HLA typing of patients and voluntary bone marrow donors and how to send these results to REDOME's information technology systems.

Aiming to answer the questions about the research and selection of donors in the systems, we inserted in this document information with reference to the SBTMO's Brazilian Consensus, published in 2021, and to the 2020 WMDA Accreditation Manual.

The accuracy of HLA typing results, as well as the correct entry of these results into the systems, is extremely important for the proper cross-referencing of these data and the identification of a donor with the indicated transplant match.

The update of the criteria for HLA typing of donors, through legislation published in 2021, should allow the optimization of the use of algorithms and search processes, reducing the time and request for complementary tests.

1. Laboratories

In order to monitor the registration regularity of the Histocompatibility Laboratories, REDOME requests the laboratories that integrate its network and perform tests for patients and voluntary donors to send the following documents annually:

- Health permit, operating license, or updated health license issued by the competent health surveillance body, in accordance with the provisions of the sole paragraph of Article 10 of Law No. 6437 of August 20th, 1977, except for complementary state or municipal legal provisions.
- Registration and cadastral status with the National Register of Health Establishments (CNES), in accordance with ANVISA RDC 61/2009. Article 12. For it to function, the Histocompatibility and Immunogenetics Laboratory must be authorized by the General Coordination of the National Transplant System - CGSNT/DAE/SAS/MS).
- Proficiency test results (External Quality Control) conducted by the Brazilian Histocompatibility Association (ABHI) or its international equivalent.
- Laboratories with recent standardization and implementation of HLA typing by NGS (Next Generation Sequencing) methodology will be requested to send the result of the standardization tests of the new methodology.
- Laboratories that have a national or international Accreditation certificate may also send these documents to REDOME.

Important: The submission of the documentation described above does not have an accreditation or certification nature, but seeks to adjust REDOME's internal processes to the best practices for donor registration, as established in the WMDA Accreditation Manual.

REDOME monitors the laboratories' performance based on indicators in a process of improvement. These data can be shared with the competent authorities - Health Secretariats and the General Coordination of the National Transplant System of the Ministry of Health - and are also available to laboratories through digital platforms or upon request.

2. HLA Typing for Donor and Patient Registration

2.1 HLA Typing for Patient Registration

Donor selection for allogeneic transplantation is first performed through HLA typing of the patient and first-degree relatives (siblings and parents) and patients who do not have compatible HLA related donors are enrolled in REDOMENET.

For the registration of patients, it is necessary to insert at least the HLA Class I (HLA-A and -B) typification in medium resolution and HLA Class II (HLA-DRB1 and - DQB1) in high resolution.

Considering the need to update and optimize the selection of unrelated donors, we suggest that the HLA typing of the patient's registry include the HLA class I and class II loci (HLA-A, -B, -C, -DRB1, DQB1, and DPB1) in high resolution.

2.2 HLA Typing for Donor Registration

For donor registration, the laboratory receives the sample from the blood center responsible for the registration and performs the HLA typing within less than 90 days. The result of the HLA typing must be made available through the REDOMEWEB system.

The HLA typing for donor registration includes the loci HLA -A, -B, -C, -DRB1, -DQB1, -DPB1 by high resolution methodology through DNA sequencing.

3. Complementary HLA Typing (Phase 2) for Donor

Donor selection for complementary HLA typing tests for donors is determined by the use of up to two international algorithms (from the NMDP American registry and the WMDA).

The laboratory responsible for donor registration must perform the test with the stored sample, as requested by REDOME through the REDOMEWEB system - HLA-C typing at medium resolution and HLA-DRB1 and HLA-DQB1 at high resolution, by molecular test. The test results must be sent to REDOME, also through this computerized system, within 14 days.

When the laboratory does not have a stored sample, this information must be included in the REDOMEWEB system and this request will be cancelled and sent again for analysis by the technical team, and may be replaced by a confirmatory typing request.

4. Confirmatory Typing (Phase 3) for Donor

The Confirmatory HLA Typing test aims to confirm the origin of the initial typing sample and the results of the donor's registry, and can also be used to include loci not evaluated in the registry.

Therefore, it must be performed with a new sample collected from the patient and the selected donor.

After the selection by the search team, the donor should be contacted by the care team in order to evaluate his/her availability and schedule the sample collection for the new typing in the blood center indicated by REDOME.

If the donor's initial HLA test has been performed in high resolution by DNA sequencing methodology and has included the loci of relevance to transplantation (HLA-A, -B, -C, -DRB1, DQB1, and DPB1), the verification test can be performed by confirmatory HLA typing by medium resolution methodology for the loci HLA-A, -B, -C, -DRB1. For medium resolution typification of the HLA-A, -B and -DRB1 loci, the confirmatory typification must be carried out, mandatorily, in high resolution by DNA sequencing methodology.

The confirmatory typing request must be received by the indicated laboratory through the REDOMEWEB system and the deadline for carrying out the tests is 21 days after receiving the sample. The results must also be sent via the computerized system.

4.1 Confirmatory Typing (Phase 3) for Patient

Confirmatory typing of the patient, in addition to confirming the origin of the result and the registration sample, is intended to optimize the unrelated donor selection and the use of search algorithms.

Thus, the confirmatory typing of the patient is requested at the moment the selection process of a compatible donor is initiated.

Currently, besides the collection of blood samples, an oral swab sample is also requested, with which the laboratory can investigate the possibility of haplotype loss (loss of heterozygosity) due to an excess of circulating blasts, which can alter the result of the HLA typing with a blood sample exclusively.

The request must be sent to the laboratory designated by REDOME via e-mail and the patient's physician is responsible for collecting and sending the samples.

The result of this test must be sent by e-mail to REDOME within 21 days from the receipt of the sample. And included by the search team in the REDOMENET system (patient's registration)

5. Delivery Term

Considering the commitment assumed with the newly registered donors and the celerity that the selection process of donors for transplantation requires, REDOME recommends the following deadlines for the release of results in the REDOMEWEB system:

- Registration HLA typing - 90 days
- Complementary HLA typing in medium resolution - 14 days
- Complementary HLA typing by high resolution methodology through DNA sequencing

6. Payment

In the registration of donors, the laboratory must perform the billing of the tests performed using the APB (Outpatient Procedure Bulletin) directly from the REDOMEWEB system.

In the case of complementary (phase 2) and confirmatory (phase 3) HLA typing, REDOME will send the request directly to the laboratory through the system and by e-mail, respectively.

Other documents may be requested by the local manager and questions regarding payment and billing should be forwarded to the Health Secretariat, responsible for payment, or to the General Coordination of the National Transplant System of the Ministry of Health.

7. Privacy and Data Security

REDOME acts to ensure the privacy of all users of its computerized systems, patients and donors, and advises that all information made available, as part of the process of identifying 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 (LGPD) - LAW No. 13,709, AUGUST 14TH, 2018.

All employees involved in this activity should be informed about the responsibility in this process.

8. Communication Channel

For further information contact the REDOME team through the following channels:

Email: rereme@inca.gov.br

Phone: (21) 3207-4733

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

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