MATCHIS
THE DUTCH CENTRE FOR STEM CELL DONORS

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Minimal criteria to access a donor and cord blood unit from the Matchis Foundation Donor Database

General

In this document the minimal criteria to access a donor or cord blood unit listed in the Matchis Foundation Donor and Cord Blood Unit database are described. These criteria comprise of

- Quality criteria for the transplant centers and acceptable transplant indications
- Provisions that are applicable when requesting a donor or cord blood unit
- Specific provisions applicable for a subsequent donation request.
- Responsibilities of the transplant centers after a request is made
- Responsibilities of the donor registry (and affiliated donor-, collection, apheresis centers and cord blood banks).

When these criteria cannot be met Matchis will consult its Medical Advisory Board to reach a decision on whether or not the request will be handled.

In this document we take into account that some or all of the responsibilities of the transplant center described in the document may have been outsourced to a transplant center coordinating unit or search coordinating unit.

Matchis Foundation is accredited by the World Marrow Donor Association and therefore adheres to the WMDA standards and where applicable the appropriate WMDA recommendations.

Matchis Foundation outsources the collection to a center licensed for Procurement by the Competent Authority. Collection and apheresis centers are JACIE accredited.

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Matchis holds a license from the Competent Authority to distribute human hematopoietic stem cells across the Dutch national border.

The transplant centers

The transplant center must be eligible or accredited with the appropriate bodies e.g. FACT, JACIE and registered with the appropriate national or international transplant outcome organization for allogeneic transplantation e.g. the European Group for Blood and Marrow Transplantation (EBMT), Center for International Blood and Marrow Transplant Research (CIBMTR).

The transplant center must be active in allogeneic HSC transplantation and must have performed for the last 2 years and plan to perform a minimum of 10 new allogeneic HSC transplants per year.

The transplant center must obtain informed consent of the patient for the transplantation according to (inter)national laws and regulations such as the WMDA standards.

It is the Transplant Center responsibility to inform the patient that the donor has the right to withdraw at any time or can be determined unsuitable to donate stem cells by the donor center.

Transplant indications

Transplant indications for which a donor can be requested for a specific patient are accepted if indicated as standard of care and clinical option by appropriate bodies such as the EBMT. Requests for donors for patients that are treated according to a procedure that is generally not recommended or that is considered experimental must be reviewed and approved by the Matchis Foundation advisory medical board. In addition a full informed consent of the donor is required.

To that end the transplant center must indicate the existence of those situations and provide detailed information about the diagnosis of the patient, the planned treatment, the experimental protocol, the scientific evidence supporting it and the prognosis of the patient.

Responsibilities during the different stages of the search process

Request considering adult stem cell donors

PRELIMINARY SEARCH STAGE

The following information must be provided by the transplant center at the preliminary search stage: HLA type of the patient, name and date of birth or age of the patient, gender diagnosis, indication if search request is an urgent or a standard search, Transplant Center or Registry information and patient ID to ensure traceability.

Matchis will not reserve the donor for that specific patient during this stage. Matchis will only perform repeat searches on request of the transplant center.

FORMAL SEARCH STAGE

The following information must be provided by the transplant center at a minimum at the formal search stage (request for a specific donor): high resolution HLA typing (A,B, C, DRB1)* of the patient (at the time of formal request for stem cell donation), name, date of birth or age, gender, weight of the patient, diagnosis and diagnosis date, stage of the disease, indication 'urgent' if applicable, donor ID, donor HLA typing, specification of required additional tests, patient ID to ensure traceability.

Matchis will reserve the donor for that specific patient, making the donor unavailable for selection by other transplant centers. The reservation period will be for a period of 90 days after a blood sample request and for a period of 14 days after the results of a typing request are available. The transplant center will be notified when the reservation period has ended and will be asked if extension of the period is needed.

FORMAL REQUEST FOR STEM CELL DONATION

In case a donor is formally requested for a stem cell donation all information as indicated on the WMDA stem cell request forms is required, including required date of clearance, duration of the conditioning, type of conditioning (myeloablative or non-myeloablative), an indication of the chance of a subsequent donation request (e.g. a lymphocytes donation) and high resolution typing of HLA-A, -B, -C and –DRB1 of the donor, if available*.

Matchis will reserve the donor for that specific patient, making the donor unavailable for selection by for other patients. The reservation will end automatically 1 year after stem cell donation.

In case the donor is considered a research subject ** the donor center must be informed by the transplant center in order for the Matchis donor registry to be able to inform the donor and to be able to obtain the applicable consent from regulatory bodies and/or review board(s). Please find a short definition of the donor as research subject in the foot notes of this document indicated by the **.

The transplant center is allowed to request samples that are needed for additional (infectious disease or other) testing. The total combined volume of these samples shall not exceed 80 mls.

The transplant center must send all results of testing performed on donor samples, such as Infectious Disease Markers and HLA-typing to Matchis.

<u>Request considering cord blood units</u>

The following information must be provided by the transplant center at the preliminary search stage: HLA type of the patient, name, gender and date of birth or age of the patient, diagnosis, indication if search request is an urgent or a standard search, name of requesting physician, Transplant Center information and patient ID to ensure traceability.

The following information must be provided by the transplant center at a minimum at the formal search stage (request for a specific cord blood unit): HLA typing (A, B, C , DRB1)* of the patient, name, gender, date of birth and weight of the patient, diagnosis and diagnosis date, stage of the disease, indication 'urgent' if applicable, CBU ID, CBU HLA typing, specification of required additional tests, patient ID to ensure traceability.

In case a cord blood unit formally requested all of the following information is required, including required date of clearance, duration of the conditioning, type of conditioning (myeloablative or non-myeloablative), all HLA-typing results of the cord blood unit as performed by the transplant center. Furthermore the transplant center is required to fill in and sign the formal request form of the Matchis Foundation specifying terms that are applicable during transport and after receipt of the unit.

The transplant center must send all results of testing performed on donor and maternal samples, such as Infectious Disease Markers and HLA-typing to Matchis.

Preference for product of an adult stem cell donor

The transplant center is asked to state their preference for the source of stem cells: from the peripheral blood or from bone marrow. The preference of the transplant center will be indicated to the donor as appropriate. Donor safety considerations or donor's personal choice may cause a donor not to be available for the requested method of stem cell collection. This will be communicated to the transplant center.

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Transport of the product

It is the responsibility of the transplant center to transport the stem cells. This responsibility starts immediately after hand-over of the product to the courier as arranged by the transplant center. It is the responsibility of the transplant center to provide import requirements and documents. Matchis Foundation will prepare the appropriate paperwork that should accompany the stem cell product as instructed by the transplant center. If the transplant center does not provide these instructions the appropriate WMDA documents are used.

The product

The product is intended solely for the purpose of immediate therapeutic treatment of the intended recipient as indicated on the request forms. Excess cells may be stored for future therapeutic treatment for this patient. No other uses of the cells are permissible. Cells not used for the therapeutic treatment of the above mentioned patient must be disposed of properly. The donor center must be provided detailed information concerning the use and/or disposal of all portions of this cell product. By accepting the product, the transplant physician also accepts these terms and conditions. Deviations from these terms are not permitted without prior written approval from the donor center.

Post donation outcome data

The transplant center must inform Matchis Foundation of any Serious Product events or adverse reactions (SPEAR) after the occurrence in accordance with the Standard Operation Procedure SEAR/SPEAR of the WMDA and within the time limits as described in this SOP. See www.worldmarrow.org.

After donation the requesting transplant center should provide regular updates on patient outcome and a one time report on product quality to Matchis Foundation. These data are requested to be able to inform the donor on request and for our quality assurance program.

Confidentiality

All donations are made anonymously and Matchis Foundation does not allow that donor and recipient will ever meet each other. Our standards do not allow any personal contact other than a once-only communication through an anonymous letter or a card. The sender must be aware that both the donor center and the transplant center are entitled to refrain from forwarding the message.

Donor informed consent and donor suitability

It is the responsibility of the donor center to obtain informed consent of the donor for the donation according to (inter)national laws and regulations such as the WMDA standards.

It is the responsibility of the collection or apheresis center to determine whether a donor is suitable to donate stem cells. The collection or apheresis center will base this decision as much as possible on applicable (inter)national guidelines. It is not allowed to communicate with the TC about the details of this decision.

It is the responsibility of the donor registry to inform the transplant center as soon as possible when it is foreseen that the product of choice cannot be delivered within the requested time frame or at all.

In case during the work-up for a PBSC collection the donor is determined to be unsuitable to donate marrow this will be communicated to the transplant center in order to make clear that there is no alternative option in case the donor is a non-mobilizer.

If there are positive findings regarding transmittable disease or deviations from standard operating procedures that may have an impact on recipient safety it is the responsibility of the transplant center to

formally accept the potential risks by signing the compassionate use declaration in case they have determined that there is no better alternative treatment for their patient.

Subsequent donations

All requests for subsequent donations must be reviewed by the Matchis Foundation Medical Advisory board. In order to review these requests at least the following information is required: reason for second donation and back-up product availability, details of the first or previous donation, graft data, patient's current condition, cancer recurrence, current laboratory data including chimerism, proposed subsequent donation type, assessment of patient survival and possibility of cure. Generally a fully completed "Previous Transplant History and Formal Request for Subsequent Stem Cell Donation" form of the WMDA will suffice.

The Medical Advisory Board will review the information provided by the transplant center within two business days after receipt of the request by the Donor Registry. The interval between the first review and reaching the decision will depend on the additional information that is requested of the transplant center. Additional information will be reviewed within one business day after receipt of that information.

The decision on acceptance of the request will be based on (published) literature on the outcome of subsequent (stem)cell therapy in comparable cases, the treatment protocol proposed, the prognosis of the patient and (transient) additional causes for the condition of the patient that may form a contra-indication for transplantation.

Minimal HLA matching requirements between patient and donor. This may differ from the matching requirements used by the transplant center for donor

selection.

The minimum HLA match requirement between patient and donor for marrow or PBSC are 7 out of 8 allele level match for HLA-A, -B, -C and –DRB1. However each of these three loci must be typed at high resolution by DNA-based methods. (Cord Blood Units excluded)

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Maximum volume or number of procedures for PBSC or marrow harvest

Donors are allowed to donate stem cells at a maximum frequency of three times in a lifetime and only a one-time PBSC donation.

Where a conventional bone marrow donation is offered the maximum volume that can be aspirated is 1500 ml or 15ml/kg donor weight, whichever is the lesser.

For a PBSC collection a maximum of two apheresis collection procedures is undertaken. Per collection a maximum of 20 liters is processed during a maximum of six hours.

If after apheresis Day 1 a second apheresis collection is indicated, the Apheresis Center physician will proceed if the donor can tolerate this and if test results are within specified ranges.

Footnotes

* Common and well-documented (CWD) alleles need to be clearly distinguished as described in Cano et al. 2007, Human Immunology 68:392-417.

** In case any part of the treatment involving the stem cell transplantation is considered research (a systematic investigation that is clearly formulated in an experimental protocol and designed to develop or contribute to generalizable knowledge) and this does involve obtaining individually identifiable donor data or donor material (e.g. cells) that will be used as part of the research the donor is considered a research subject. From: RJ King, DL Confer, HT Greinix et al Unrelated Donors as a Research Subject, BMT (2011) 46, 10-13.