DKMS✕ Registry

EMDIS NATIONAL RULES

DKMS Registry

Version 5, valid as of 2021-09-13
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Introduction

This document outlines the specific implementation of EMDIS in the DKMS Registry. It is intended for use by EMDIS network partners to understand the processes at DKMS Registry and their effect on message exchange in the EMDIS framework.

Level of Implementation

Message	Incoming	Outgoing
ADMIN	n/a	n/a
ALM_REQ	NO	NO
ALM_RES	NO	NO
CBR_REQ	n/a	YES
DONOR_CB	YES	YES
IDM_REQ	YES	YES
IDM_RES	YES	YES
MARR_STAT	NO	NO
MATCH_SUM	YES	YES
MSG_ACK	YES	YES
MSG_DEN	YES	YES
NEW_ADD	YES	YES
NO_RES	YES	YES
PAT_STAT	YES	YES
PAT_UPD	YES	YES
PHEN_LIST	YES	YES
REQ_CAN	YES	YES
RES_REM	YES	YES
RSV_REQ	YES	YES
RSV_RES	YES	YES
SMP_ARR	YES	YES
SMP_REQ	YES	YES
SMP_RES	YES	YES
SMP_INFO	YES	YES
TXT_MSG	YES	YES
TYP_REQ	YES	YES

TYP_RES	YES	YES
WARNING	YES	YES
WOR_REQ	NO	NO

Search Algorithm

The search algorithm used at DKMS Registry is called Hap-E Search (Haplotype-Enhanced Search). Hap-E Search is a probabilistic search algorithm based on haplotype frequencies and was developed by DKMS in 2012. Where only incomplete HLA typing information is available, haplotype frequencies are used to estimate the probability that a specific donor is a match. The algorithm currently uses 29,334 German, Turkish, Polish, Italian, Russian and Indian HLA-A, -B, -C, -DRB1, and -DQB1 haplotype frequencies, depending on donor's and patient's descent. Hap-E Search predicts the 10/10, 9/10 and 8/10 matching probability of a donor, i.e. the probability that there are no, one or two allele-level mismatches between donor and patient. Potential 9/10 and 10/10 matched donors are selected based on antigen recognition site matching (WMDA AI3). Hap-E Search has been validated in the WMDA matching validation project (Bochtler et. al, 2011, 2013, 2016).

Patient and Donor Administration

The DKMS Registry lists unrelated stem cell donors from India (DKMS BMST Foundation India, ION-9935), Chile (Fundación DKMS, ION-1574), United Kingdom (DKMS Foundation United Kingdom, ION-9968), Poland (Fundacja DKMS, ION-7414) and Germany (DKMS gemeinnützige GmbH, ION-5525).

Please note:

- DKMS requires, that EMDIS partners have processes in place to evaluate experience and equipment of Transplant Centers to perform matched / mismatched unrelated donor transplantations.
- No cord blood units are available via EMDIS from the DKMS Registry. Requests for cord blood units and the respective messages and codes are ignored when a search inquiry is processed.
- Data provided on the patient's ethnic group and on the grafting physician's identification are not evaluated.

- Serological HLA typing results for patient data are generally not accepted. At a minimum antigen and/or allele value for the HLA loci HLA-A, -B, and -DRB1 must be provided with the PAT_UPD messages. Best matching results are achieved when at least HLA loci HLA-A, -B, -C, -DRB1, -DQB1 are provided. If the patient's HLA data is not provided in high resolution, a WARNING is issued.
- Before sending a request, HLA data should be provided in high resolution.
- DKMS Registry rejects any HLA information submitted using HLA Nomenclature Versions prior to 3.x.
- DKMS Registry maintains a strict policy on provision of stem cell products to patients with clear indication for HSCT. Therefore, each patient case is evaluated with respect to the patient's age and diagnosis. The following process applies:

  o For patients over the age of 80, additional information may be required regarding, for example, therapy protocol, comorbidities or IRB approval may be required. A final decision about clearance from our medical advisor is required before a workup request can be processed.
  o DKMS maintains an internal list of diagnosis cleared for unrelated donor provision for HSCT by our medical advisors. Therefore, you may be asked for a specific patient diagnosis and possibly more details on the therapeutic protocol. A final decision about clearance from our medical advisor is required before a workup request can be processed.

Matching Preference

DKMS Registry provides 10/10 and 9/10 matching results only. Mismatches are evaluated according to published WMDA matching criteria on antigen recognition site identical alleles. The direction of mismatches (GvH/HvG) is not evaluated.

Donors with more than one mismatch can be sent via EMDIS upon request to services@dkmsregistry.org .

DKMS Registry always performs a 10/10 or 9/10 search, where the mismatch can be on any locus (A, B, C, DRB1 or DQB1), regardless of the P_MATCH_DR or P_MATCH_AB parameter. In particular, no locus is ignored in the search. Then the requested filter criteria as specified in the P_MATCH_DR string are applied following DKMS Registry implementation (see below) and results are sent out accordingly.

Not all settings for the matching preferences (P_MATCH_AB / P_MATCH_DR), which are possible according to EMDIS semantics, are accepted by DKMS Registry:

- The first position of the string will be ignored by us (=HvG mismatches are not ignored).
- Values specifying the total number of mismatches in (position 3, 6, 9, 11, 13, 15, and 17 of the MP string) are ignored. For mismatches at antigen recognition sites of the loci, a maximum of one mismatch is accepted. If a higher number is requested, it is automatically reset to one.
- DKMS Registry accepts all possible values for the value filter part (HLA-C, HLA-DQ, HLA-DPB1, gender, CMV-status).
- The third part of the MP string is not processed.

Examples for P_MATCH_DR

Incoming P_MATCH_DR	Outgoing P_MATCH_DR
0:XX:61:**21**21**X**X**21X**X**/**	0:11:11:1**111111111**/
0:XX:61:**21**21**X**X**20X**X**/**	0:11:11:1**111110011**/
0:XX:60:**20**20**X**X**20X**X**/**	0:11:00:0**000110011**/

P_MATCH_CB is silently ignored and is not processed as DKMS Registry does not list any cord blood units.

If P_MATCH_AB / P_MATCH_DR are missing or are blank, the following default values are used:
P_MATCH_AB= 0:11:00:0000111111/ and
P_MATCH_DR= 0:11:11:1111111111/.

Repeat Search Program

Search updates for patients with status active (ACT) are run daily (overnight, Central European Time). Remote registries are requested to set the status of registered patients to suspended (SUS) or stopped (STP) once regular search updates are not needed anymore. For cases, which are inactive for longer than 185 days, the repeat search is stopped. However, any patient related message via EMDIS re-activates the daily repeat search for the patient.

Requests

Incoming Sample Request [SMP_REQ, SMP_RES, SMP_ARR]

Please note the following national rules:

- The amount of blood samples requested for verification typing (SMP_REQ) must not exceed 50 ml. If more than a total of 50 ml is requested, an explanation is required and authorization from the registry/donor center, where the donor is registered, is needed. A WARNING is sent accordingly.
- There is no guarantee, that blood samples is provided exactly as requested. Number, volume of tubes and in rare cases the anticoagulant may differ from the placed order due to the availability of certain types of tubes.
- If no volume quantity is specified, a tube containing 10 ml of blood with the specified reagents is sent as standard. Request are not processed for which the volume, but not the reagent is specified. A WARNING is sent.
- Requests for tubes with Citrate Phosphate Dextrose (CPD) as anticoagulant are not be processed as CPD cannot be provided. A WARNING is sent.
- Duplicate orders are joined and treated as one request.
- REC_DATE1 and REC_DATE2 are ignored.
- Once the date of blood draw has been scheduled, the donor is automatically reserved for this patient for 90 days.

The screening for infectious disease markers is included in a sample request (SMP_REQ). It comprises routinely:

- HBsAG, Anti-HBc, Anti-HIV, Anti-HCV, Anti-CMV (IgG + IgM) and STS (Lues), as well as the testing of the ABO blood group and Rhesus factor.
- For donors from India (ION-9935) a test for Malaria QBC is performed in addition.
- For donors from Chile (ION-1574) antibodies to Trypanosoma cruzi (IgG, Chagas) are tested in addition.

    The results of Malaria and Chagas tests are shared via TXT_MSG.

Incoming Typing Request [TYP_REQ, TYP_RES]

All requested loci are typed in high resolution by molecular methods. Except HLA-DRB3, HLA-DRB4 and HLA-DRB5, all other loci can be request individually. The donor is not automatically reserved for the patient after a typing request.

Incoming Request for Infectious Disease Markers [IDM_REQ, IDM_RES]

The following infectious disease markers can be requested:

- HBsAG, Anti-HBc, HBV-NAT, Anti-HCV, HCV-NAT, Anti-HIV, HIV-NAT, STS (Lues), Anti-CMV (IgG + IgM), Anti-HTLV I/II), Anti-EBV (IgG + IgM) and Anti-Toxoplasmosis (IgG + IgM).
- For donors from India (ION-9935) testing for Malaria QBC is possible in addition.
- For donors from Chile (ION-1574) antibodies to Trypanosoma cruzi (IgG, Chagas) are also tested.

Workup Request

Messages related to Workup requests are not dealt via EMDIS. Workup requests have to be sent to the DKMS Registry for all donor pools (ION-9935, ION-1574, ION-9968, ION-7414 and ION-5525). You may use respective WMDA forms for Workup request, subsequent donation request or request for MHC Apheresis.

Contact: workup@dkmsregistry.org or send a fax to +49 7071 943 2299.

Cord Blood Units

DKMS registry does not provide CBUs. Messages relating to cord blood units are not processed.

KIR typing

In our lab the typing of KIR loci 2DL5A and 2DL5B cannot be separated. Sometimes it is known that only one locus is present but it cannot be determined which one. In this situation, we send POS for both loci.

Invoicing

Invoicing address is

DKMS Registry gGmbH
Kressbach 1
72072 Tübingen
Germany

Invoices received from DKMS Registry must be paid within 30 days, otherwise dunning charges may apply.

References

Bochtler W, Maiers M, Bakker JNA, Oudshoorn M, Marsh SGE, Baier D, Hurley CK, Müller CR on behalf of the Information Technology Working Group of the World Marrow Donor Association. (2011) World Marrow Donor Association framework for the implementation of HLA matching programs in hematopoietic stem cell donor registries and cord blood banks, Bone Marrow Transplantation, 46:338-343.

Bochtler W, Maiers M, Bakker JNA, Baier DM, Hofmann JA, Pingel J, Rist HG, Oudshoorn M, Marsh SG, Müller CR, Hurley CK, Information Technology Working Group of the World Marrow Donor Association. (2013). An update to the HLA Nomenclature Guidelines of the World Marrow Donor Association, 2012., Bone Marrow Transplantation, 48:1387-8.

Bochtler W, Gragert L, Patel ZI, Robinson J, Steiner D, Hofmann JA, Pingel J, Baouz A, Melis A, Schneider J, Eberhard HP, Oudshoorn M, Marsh SGE, Maiers M, Muller CR. (2016) A comparative reference study for the validation of HLA-matching algorithms in the search for allogeneic hematopoietic stem cell donors and cord blood units. HLA, 87:439-448. doi:10.1111/tan.12817