

POLICY STATEMENT

This policy outlines the minimum requirements for HLA Confirmatory Typing (HLA-CT) of patients and allogeneic cord blood units (CBU) from the Be The Match Registry. This policy is meant to apply to those situations when the HLA-CT is within the control of the Be The Match Registry or the transplant center; for other situations, the policy may serve as a recommendation for best practice.

BUSINESS SECTION/DEPARTMENT

Repository and Laboratory Services Department

PURPOSE

This policy is meant to verify and ensure that the unit being selected and shipped to the transplant center is the source of the HLA assignment determined at the time of banking. This policy is not meant to be used as a requirement to define final recipient and CBU match criteria. Transplant centers may decide to consider typing for additional HLA loci (e.g., DQB1, DPB1) or resolve alternative HLA assignments that remain after HLA-CT requirements are met.

SCOPE

This policy applies to National Marrow Donor Program (NMDP) personnel and, where relevant, the NMDP Network. The policy content additionally may extend to other entities and persons, pursuant to contact.

RELATED DOCUMENTS

[Form 117](#): available on the Network Web Site

DEFINITIONS

Not applicable

RESPONSIBILITIES

Repository and Laboratory Services Department: develop and manage policy, publish/post policy so that it may be accessed by affected audiences.

REQUIREMENTS

Sample and Timing Requirements

HLA-CT of a CBU must be carried out using a sample from a segment attached to the CBU. The attached segment must be removed from the unit at the time of the HLA-CT request. When segment material is not available for CT, HLA typing should be performed on ancillary material; while useful, ancillary typing is not confirmatory typing.

HLA-CT of the potential recipient should be performed on a second independent sample prior to CBU shipment and/or patient conditioning; preferably, results will be submitted at the time of the CBU shipment request.

Use of CBUs with no Available Attached Segment for HLA Confirmatory Typing

For a CBU to be used when there is no attached segment available for HLA-CT and HLA-CT has not previously been performed, a minimum typing of HLA-A, B, and DRB1 should be performed on a sample from the bag itself at a resolution sufficient to determine concordance with registry typing before the infusion of HPC, Cord Blood.

HLA Typing Requirements

HLA-CT must be reported on both the CBU and recipient and include assignments for HLA-A, B, C, and DRB1. Either the HLA-CT or the prior HLA typing must be performed at a resolution consistent with the following criteria:

The common and well-documented (CWD) alleles, including CWD null alleles, that need to be clearly distinguished in order to meet the criteria for high resolution are described in the 2013 manuscript by Mack et al. 2013 (referenced below) or the most current published update to the CWD list. The CWD listing can be accessed at <http://igdawg.org/cwd.html>.

The NMDP **does not** require the resolution of CWD alleles within G groups (defined at <http://hla.alleles.org>). However, laboratories **are** required to test for the following non-expressed alleles when they exist as a possibility within the assigned G group. A list of these null alleles within G groups is provided below.

Null Allele	HLA G Group	Location of Polymorphism
A*01:04N	A*01:01:01G	Exon 4
A*03:21N	A*03:01:01G	Exon 4
A*24:09N	A*24:02:01G	Exon 4
A*24:11N	A*24:02:01G	Exon 4
A*68:11N	A*68:01:02G	Exon 1
B*15:01:01:02N	B*15:01:01G	Intron 1
B*51:11N	B*51:01:01G	Exon 4
C*04:09N	C*04:01:01G	Exon 7

If the HLA-CT does not meet the resolution requirements, additional documentation of prior HLA typing that does meet the resolution requirements must be submitted.

Reporting Results to the NMDP

Final reporting of high resolution HLA typing results must meet **one** of the following criteria:

- 1) must contain only one unambiguously assigned genotype or
- 2) may contain multiple alternative genotypes if one includes two CWD alleles and the others do not include any alleles listed as CWD with the following exceptions:
 - a. Laboratories are not required to resolve CWD alleles within an HLA region that encodes identical protein sequences in the antigen recognition site (i.e., G assignment) with the exception of CWD null alleles as described above.
 - b. When **alternative genotypes** include combinations with **one CWD allele plus an allele not designated as CWD**, the resolution to a single genotype may not be required. If the laboratory possesses information or data relevant to the particular ambiguity being evaluated which provides evidence that the resolution to a single genotype may not be required, the laboratory may decide to claim a deviation from this policy and to report the result as completed.

Important to note: there have been numerous cases submitted to the NMDP and to the American Society for Histocompatibility and

Immunogenetics demonstrating the clinical relevance of resolving these types of ambiguities. Therefore, it is highly recommended that laboratories critically evaluate each case and resolve these alternative genotypes as appropriate. This decision must be documented by the Laboratory Director and communicated to the NMDP together with the final typing results.

Along with other required forms, submission of patients' final laboratory reports to document decisions made or to supplement final HLA typing results being reported is highly encouraged. The laboratory report must clearly include **all** unresolved ambiguous HLA assignments.

HLA laboratories must continue to adhere to all other accrediting agency standards and policies associated with high resolution DNA typing as defined by the American Society for Histocompatibility and Immunogenetics, the College of American Pathologists, or the European Federation for Immunogenetics.

REFERENCES

Common and Well-Documented HLA Alleles: 2012 update to the CWD catalogue.

Mack SJ, et al. 2013. Tissue Antigens 81(4):194-203. A copy of the manuscript and a listing of CWD alleles can be accessed at <http://igdawg.org/cwd.html>.

An electronic copy of this policy can be found at the NMDP Bioinformatics Website:

<http://bioinformatics.nmdp.org/Policies/Policies.aspx>

REVISION HISTORY

Revision	Brief Description of Revision
P00080 rev. 1	Created separate policy for CBUs. Reflects current HLA typing requirements.