NMDP Policy for Confirmatory Typing Requirements Effective May 1, 2009

This policy outlines the minimum requirements for Confirmatory HLA Typing (CT) of patients and unrelated volunteer adult donors. This policy is **not** meant to be used as a requirement to define final patient and donor match criteria. Transplant centers may decide to consider typing for additional HLA loci (i.e., DQB1, DPB1) or to resolve alternative HLA assignments that remain after the NMDP CT typing requirements are met.

High Resolution HLA Typing

High resolution HLA-A, B, C and DRB1 typing must be performed and reported on both the patient and all primary and back-up donors **requested for work-up** before a stem cell collection can proceed. In accordance with ASHI policies for proficiency testing, the definition of an acceptable result and the common and well-documented (CWD) alleles that need to be clearly distinguished in order to meet the criteria for "high resolution" are described in the 2007 manuscript by Cano et al (referenced below).

The NMDP agrees with the recommendation that laboratories **are not** required to resolve CWD alleles that encode identical protein sequences in the antigen recognition site. However, laboratories **are** required to test for the following three (3) CWD null alleles when alleles and/or haplotypes that have been associated with the specific null alleles exist.

Null Allele	Alternative Common Allele	Associated Alleles in Haplotype	Location of Polymorphism
A*2409N	A*24020101	**B*40 or B*27**	Exon 4
B*5111N	B*510101	**A*0201 and DRB1*0402 and Cw*15BJ**	Exon 4
Cw*0409N	Cw*04010101	**B*4403**	Exon 7

Serology may be used as an alternative to testing for the DNA polymorphism defining these null alleles. This approach should only be used in cases where the serology clearly distinguishes the expected specificities at the relevant locus. The final results of **both** the DNA and serology testing must then be reported to the NMDP.

Reporting Results to the NMDP

A. Summarizing the requirements detailed in the manuscript, final reporting of high resolution HLA typing results must meet **one** of the following criteria:

1) must contain only one unambiguously assigned genotype.

2) may contain multiple alternative genotypes if one includes two CWD alleles, and the others do not include any alleles listed in the tables from Cano et al, with the following exceptions:

- Laboratories are not required to resolve CWD alleles that encode identical protein sequences in the antigen recognition site.

- When **alternative genotypes** include combinations with **one CWD allele plus a rare allele** (see two examples in following chart), 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.

  On the other hand, there have been numerous cases submitted to the NMDP and to ASHI 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 reported on the completed Form 22 and/or 117.

B. You are encouraged to submit final laboratory reports, along with other required forms, to document decisions made or to clarify final HLA typing results being reported. Additionally, the laboratory report must clearly include **all** unresolved alternative assignments. HLA laboratories must continue to adhere to all other accrediting agency standards and policies associated with high resolution DNA typing as defined by ASHI or EFI.

Reference:

Common and Well-Documented HLA Alleles: Report of the Ad-Hoc Committee of the American Society for Histocompatibility and Immunogenetics. Cano P, et al. Human Immunology 68, 392-417 (2007). Please refer to the publication for a complete listing of alleles, discussion and valuable examples.

An electronic copy of this policy can be found at the NMDP Bioinformatics Website: http://bioinformatics.nmdp.org/POLICIES/policies_idx.html.

Few Representative Examples of Multiple Genotype Results

Genotype Results	Example	Resolution	Testing
CWD1, CWD2 **Rare1, Rare2**	B*3501 (CWD), B*4601(CWD) B*3562 (Rare), B*4608 (Rare)	**Acceptable**	**Complete**
CWD1, CWD gi [a] **CWD1, CWD gi**	B*1502, B*070501 (B*070501g allele group) B*1502, B*0706 (B*070501g allele group)	**Acceptable**	**Complete**
CWD gi, CWD gf [b] **CWD gi, CWD gf**	B*1503, B*4001 B*9503, B*4055	**Acceptable**	**Complete**
CWD gi, Rare1 **CWD gi, Rare1**	B*070501, B*4044 B*0706, B*4044	**Acceptable**	**Complete**
Includes different CWD alleles			
CWD1, CWD2 **CWD3, CWD4**	B*3501, B*4901 B*5001, B*5301	**Not Acceptable**	**Perform Additional Testing**
Does not include CWD alleles			
Rare1, Rare2 **Rare3, Rare4**	A*3107, A*3309 A*3110, A*3308	**Not Acceptable**	**Perform Additional Testing**
Includes one or more genotype possibilities containing only one CWD allele			
** **CWD1, CWD2** **CWD1, Rare1** (** **see discussion for exception policy)**	DRB1*1104, DRB1*1301 DRB1*1104, DRB1*1351	**Not Acceptable**	**Perform Additional Testing**
** **CWD1, CWD2** **CWD3, Rare1** (** **see discussion for exception policy)**	A*250101, A*6601 A*2502, A*6605		
CWD1, Rare1 **CWD2, Rare2**	A*0202, A*0251 A*0205, A*0240		
Includes one or more genotype possibilities involving groups of alleles that have identical ARS sequences			
CWD gi, CWD1 **CWD gi, CWD1** **CWD2, CWD3**	B*15BKVK, B*1502 B*1515, B*1525	**Not Acceptable**	**Perform Additional Testing**
CWD gi, CWD gf **CWD gi, CWD gf** **CWD2, CWD3**	B*07EH, B*35BEZX B*0709, B*3504		
CWD gi, Rare1 **CWD gf, Rare2**	B*07CVAC, B*4414 B*07EH, B*4451		

[a] CWD gi = allele group of CWD alleles with identical ARS sequence
[b] CWD gi, gf = two different groups of CWD alleles with identical ARS sequence