NMDP Policy for Handling Recent HLA Nomenclature Changes and Notice of Upcoming NMDP Allele Code Character Expansion

February 2003

1. **Extension of Nomenclature to Describe Synonymous Mutations**

   In 1990 a fifth digit was added to the naming convention of a four digit code to distinguish HLA alleles that differ in the proteins they encode to permit the distinction of sequences differing only by synonymous (non-coding) nucleotide substitutions within the exons (e.g., A*02011). Recently, the decision was made to introduce an extra digit between the current fourth and fifth digit to allow up to 99 synonymous variants of each allele (e.g., A*020101). This expands the full allele name to eight digits when describing an allele when both synonymous variation and variation in introns or 5´ or 3´ regions of the gene are observed (S.G.E. Marsh, et.al.).

   Within the NMDP database, the synonymous mutation fields will be represented with 1 character whenever possible (e.g., A*02011) and will not be extended to 2 characters at this time. This decision was made on the basis of the following reasoning: (1) laboratories will not be explicitly typing for these synonymous variations in most cases; (2) there are no allele codes for synonymous mutation containing combinations; (3) this is currently an optional field that is not used in the matching algorithm; and (4) as the trend toward capturing primary (SSO/SSP/SBT) HLA data continues, the interpretation of this data will be based on current nomenclature and will consider all synonymous mutations.

2. **Renaming of HLA Alleles**

   The names of three class I alleles have been changed effective as of October 2002.

   - **A*2416 renamed A*3108**
   - **B*1522 renamed B*3543**
   - **B*1559 renamed B*3544**

   The NMDP has activated all three of these allele names in our system and is prepared to accept the new names and can create allele codes containing these new allele names. We will continue to accept HLA typing results that contain the old allele names, as well as the allele codes containing them, until **May 2, 2003**. At that time the old allele names, and all codes containing them, will be inactivated. From that point in time, only HLA typing results using the new allele names and associated allele codes will be accepted into our system.

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3. **Naming of Alleles With Aberrant Expression**

The addition of an optional "N" or "L" suffix to an allele to indicate either "Null" or "Low" expression was introduced in previous nomenclature reports. All alleles containing "null" mutations are stored in our system with an "N" in the fifth digit (e.g., A*0215N or B*1501N). These five digit allele names are also used when allele codes are created for allele combinations containing null alleles. The **A*24020102L** allele will be named **A*2402L** in our system, and allele codes defining combinations containing this allele will be created upon request. Additionally, the A*2402L allele will be searched with the assigned search determinant (SD) of "24".

A new allele suffix "S", created and described in the 2002 WHO Nomenclature report (S. G. E. Marsh, et.al.), denotes an allele specifying a protein that is expressed as a soluble "Secreted" molecule, but is not present on the cell surface. The first example of a secreted only HLA molecule is that encoded by the newly assigned **B*44020102S** allele. In keeping with the NMDP's internal naming convention for alleles exhibiting aberrant expression, the **B*44020102S** allele will be named **B*4402S** in our system, and allele codes defining combinations containing this allele will be created upon request. The B*4402S allele will be searched with the assigned search determinant (SD) of "blank", which is the SD assignment given to all "Null" alleles.

4. **Expansion of NMDP Allele Codes to Four Characters**

The NMDP uses allele codes to facilitate the reporting of intermediate resolution HLA typing results. The combination of possible alleles at a given locus is currently represented by either a 2 or 3 character letter code (e.g., **B*15RXW** = 1503/1518/1564). At the current rate of allele code assignment, the NMDP will use all remaining 3 character codes as early as July 2003 and will need to expand the codes used to **4 characters** in order to continue to capture all HLA typing results submitted to the NMDP.

Reference: **Nomenclature for factors of the HLA system, 2002**
S.G.E. Marsh, et.al, Tissue Antigens (2002) 60 407-464

**HLA Resources on the NMDP Research Web Site
http://www.nmdpresearch.org/HLA/hla_resources_idx.html**