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HLA Standards Document

1. WMDA approved HLA typing requirements

1.1. WHO HLA Nomenclature Committee approved codes

1.1.1. Serologic broad, split and associated antigen assignments

Examples:

Acceptable: A2, A203, DR6

Unacceptable: C13, DR'Bon'

Remark:

Inclusion of the broad designation when listing the split is not allowed.

Example: DR13(6) must not be used, but DR13

1.1.2. Allelic assignments

Examples:

Acceptable: B*15010101, DRB1*0103, B*1594N

Unacceptable: B*6201, DRB1*0601, B*1594

Remark:

Inclusion of the accompanying expression level character specifying a non or low expressed allele is required for registry communication.

Remark:

HLA assignments using older forms of nomenclature that once had been approved but were subsequently altered are not acceptable assignments and have to be changed.

Examples:

A*2401 has been deleted

B*7901 has been renamed to B*1518 (individual)

DRB1*11011 has been renamed to DRB1*110101 (rule based)

Notes:

- The WHO HLA Nomenclature Committee approved codes are listed on the WMDA designated reference web site:
<http://www.anthonynolan.org.uk/HIG/nomen/wmda.html>
- All entries on the reference web site are assigned a first and, if applicable, a last validity date.
- Changes must be announced on the reference web site and will become valid 48 hours later.

- 1.2. Codes derived from WHO Nomenclature Committee approved allele designations.
- 1.2.1. Shortened forms of WHO Nomenclature Committee approved allele designations in which only digits 1-4 or 1-6 and optionally an existing expression level character is included. No other abbreviations are allowed.

Remark:

Preservation of the accompanying expression level character specifying a non-expressed or low expression allele is required for registry communication.

Notes:

- A shortened code without trailing expression level character includes all alleles which are prefixed by the digits of the shortened code without regard of specific expression levels.
- A shortened code with trailing expression level character includes all alleles which are prefixed by the digits of the shortened code and are of the appropriate expression level. It does not imply that there aren't any alleles prefixed by the digits of the shortened code with different expression levels.

Examples¹:

DRB1*1101 includes

DRB1*110101 or DRB1*110102 or DRB1*110103 or DRB1*110104

B*1501 includes

B*15010101 or B*15010102N or B*150102 or B*150103 or B*150104

B*150101 includes

B*15010101 or B*15010102N

B*1501N or B*150101N includes

B*15010102N

A*2402 includes

A*24020101 or A*24020102L or A*240202 or A*240203 or A*240204 or A*240205 or A*240206

A*240201 includes

A*24020101 or A*24020102L

A*2402L or A*240201L includes

A*24020102L

¹ according to the data on the reference web site as of May 1, 2005

1.2.2. Family codes derived from WHO Nomenclature Committee approved allele designations in which only digits 1-2 trailed with 'XX' are included.

Examples:

Acceptable: DRB1*11XX, B*15XX

Unacceptable: DRB1*18XX, B*62XX

Unacceptable: Broad family codes A*09XX, A*10XX, A*19XX, A*28XX, B*05XX, B*12XX, B*16XX, B*17XX, B*21XX, B*22XX, DRB1*02XX, DRB1*05XX, DRB1*06XX, DQB1*01XX

These are not allowed for registry use and should be replaced with the appropriate multiple allele code

Note: New roll-over alleles such as A*9201 or B*9501 should be considered as being included in their corresponding family codes A*02XX and B*15XX respectively. A*92XX and B*95XX are not allowed.

1.3. WMDA approved additional codes

1.3.1. Special codes

NNNN only for DRB3/4/5 (negative)

XXXX only for DRB3/4/5 (positive)

UUUU only for CT results (undone)

1.3.2. Multiple allele codes

The NMDP multiple allele code definitions must be used to handle ambiguous typing results. To avoid confusion, no other coding system is currently allowed.

Remark:

The current set of multiple allele codes is determined by the current NMDP code definitions based on the current WHO Nomenclature Committee approved allele designations.

Examples:

Acceptable: DRB1*11AD, representing the possibilities DRB1*1101/1104

Unacceptable: DRB1*02AD, because there are no DRB1*02 alleles

Note:

The NMDP code definitions for multiple allele possibilities are listed on the WMDA designated reference web site:

http://www.nmdpresearch.org/HLA/allele_code_lists.html

2. WMDA approved phenotype specific requirements

- 2.1. Laboratories must assign DNA nomenclature to results obtained using DNA based methods and serologic nomenclature to results obtained using antibody reagents.
 - 2.1.1. The practice to convert alleles to antigens for technical reasons related to matching programs should be abandoned as soon as possible.
 - 2.1.2. Only actual typing assignments and no derived values should be exchanged.
- 2.2. IT systems must provide separate fields for antigen and allele assignments, e.g. for DR and DRB1. Either one or both fields may be filled with typing information.
- 2.3. A maximum of two antigen or two allele assignments can be provided for each locus. For example A2,A3,A11 would not be accepted in the antigen assignment field.
- 2.4. If the identity of an antigen is unknown it is recommended to use DNA based typing to clarify the assignment. The code X may not be used to indicate unclear serologic assignments. For example A2, X will not be accepted.
- 2.5. If corresponding antigen and allele assignments are available, the number of entries must not differ except in one of the following cases
 - 2.5.1. One of the two alleles is non or low expressed
e.g. B*0704, B*1501N corresponds to B7 only
 - 2.5.2. One of the two alleles does not have a corresponding antigen
e.g. Cw*0103, Cw*1205 corresponds to Cw1 only
 - 2.5.3. Both alleles correspond to the same antigen
e.g. DRB1*1101,DRB1*1104 corresponds to DR11 only
 - 2.5.4. A single allelic code designation is an appropriate multi allele assignment for both antigens e.g. B*15XX only corresponds to B62, 75

Note:

The WHO HLA Nomenclature Committee approved correspondencies between antigens and allele assignments are listed on the WMDA designated reference web site: <http://www.anthonynolan.org.uk/HIG/nomen/wmda.html>

- 2.6. Individuals tested as carrying a single HLA antigen or allele must be listed as the single assignment only unless family segregation studies have been used to indicate that two copies of the type are present:
 - 2.6.1. The single assignment must be accompanied by an empty field. Any other symbol or letter code as a placeholder to indicate the single assignment is not allowed, e.g. A2 only and not A2, 2 or A*0202 only and not A*0202, A*0202
 - 2.6.2. The empty field should be treated as either a blank (meaning unknown type) or as a homozygote.
 - 2.6.3. It is acceptable to map donors with two identical assignments at a locus (homozygous) back to one single assignment since it is unlikely that segregation information is available on donors and since matching programs are unlikely influenced by that.
 - 2.6.4. It is explicitly discouraged to map patients with two identical assignments at a locus (homozygous) back to one single assignment because this is regarded as a loss of information.
- 2.7. A CT result including one untested allele assignment has to be reported using the special code UUUU. Such a result can only be accepted in the following cases:
 - 2.7.1. A complete and consistent serologic typing is known beforehand or provided within the result, e.g. DR1,4 along with DRB1*UUUU, DRB1*0401
 - 2.7.2. A complete and consistent low resolution allele assignment is known

beforehand, e.g. DRB1*01XX, DRB1*04XX prior to DRB1*UUUU, DRB1*0401

2.8. Concerning secondary DRB loci, i.e. DRB3/4/5

- 2.8.1. Secondary DRB loci assignments are not required.
- 2.8.2. Typing one secondary DRB locus does not imply that the other secondary DRB loci have been tested.
- 2.8.3. Typing a secondary DRB locus with no allele subset designated can be reported using the special code XXXX.
- 2.8.4. Typing a secondary DRB locus which shows the absence of any allele can be reported using the special code NNNN.
- 2.8.5. More than two alleles present in one or more of the three secondary DRB loci should be regarded as implausible and generate a warning.
- 2.8.6. Rare DRB1-DRB3/4/5 combinations may be flagged but should not be rejected. The overall frequency of such uncommon combinations should be monitored as part of quality assurance measures.
- 2.8.7. Secondary DRB loci assignments may be used – when present – as a check for the two digit DR or DRB1 assignment:
 - DRB3 pos. typing (or DRw52) should include at least one DR3, 11, 12, 13 or 14 assignment.
 - DRB4 pos. typing (or DRw53) should include at least one DR4, 7 or 9 assignment.
 - DRB5 pos. typing (or DRw51) should include at least one DR15 or 16 assignment.

It should be noted that exceptions to these associations do exist (e.g. DR15 without DRB5 and vice versa) so DRB locus associations should only be used to generate warnings but not as a data filter.

Revision History

Version 0.7 May 23, 2003	Carolyn Hurley based on Dreieich IT discussion and further comments from IT
Version 0.8 Nov 11, 2003	Martin Maiers based on feedback from WMDA IT/WG
Version 0.9 Mar 3, 2004	Martin Maiers based on feedback post Minneapolis IT/WG meeting
Version 0.91 Mar 18, 2004	Updates by Carolyn Hurley and comments from Machteld Oudshoorn
Version 0.92 Mar 23, 2004	Format changes by Martin Maiers
Version 0.93 Mar 24, 2004	Restructured (based on v0.9) by Werner Bochtler
Version 0.99 Oct 08, 2004	Barcelona Meeting (March 26, 2004) and v0.91-2
Version 1.0 Oct 27, 2004	Feedback from WMDA/IT closed meeting
Version 1.01 Nov 08, 2004	Final input from WMDA/IT open meeting
Version 1.02 Apr 17, 2005	Updates by Werner Bochtler based on email discussion
Version 1.03 Mai 11, 2005	Comments from Machteld Oudshoorn New section 2.5.2 by Werner Bochtler Unification and correction of locus designations based on email discussion by Werner Bochtler
Version 1.04 Mai 11, 2005	Comments from Machteld Oudshoorn