

Terminology Terminologie

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Nomenclature for factors of the HLA system, 1977*

This article gives the decisions of the WHO nomenclature committee on leukocyte antigens, in particular concerning (a) the upgrading of certain HLA-A and HLA-B specificities to full HLA status, (b) the designation of new provisional specificities of the HLA-B, HLA-C, and HLA-D loci, and (c) the establishment of a nomenclature for the new specificities identified by serological techniques on B lymphocytes.

The WHO nomenclature committee on leukocyte antigens met under the auspices of the World Health Organization and the International Union of Immunological Societies, after the 7th Workshop on Histocompatibility Testing in Oxford in September 1977, with the aim of updating the nomenclature for specificities of the HLA-A, HLA-B, HLA-C, and HLA-D loci and establishing a nomenclature for the new specificities identified by serological techniques on B lymphocytes.

Previous reports in the *Bulletin of the World Health Organization* (1, 2, 3) have established a revised nomenclature for the HLA region. Taking into account advances in knowledge of the genetics of the major histocompatibility system of man it was agreed that HLA should be the name given to the whole region, while the terms HLA-A, HLA-B, HLA-C, and HLA-D should refer to the individual loci within it. Numbers following the locus symbols would identify individual specificities (e.g., HLA-A1), while the letter w following the locus symbol and preceding the number would indicate a provisionally identified specificity (e.g., HLA-Bw35).

The main aims of this report are:

(1) to upgrade certain HLA-A and HLA-B locus specificities to full HLA status.

Table 1. New designations for specificities of the HLA-A and HLA-B loci that have been upgraded to full HLA status

New	Previous
HLA-A25	HLA-Aw25
HLA-A26	HLA-Aw26
HLA-B15	HLA-Bw15
HLA-B17	HLA-Bw17
HLA-B37	HLA-Bw37
HLA-B40	HLA-Bw40

(2) to designate new provisional specificities of the HLA-B, HLA-C and HLA-D loci.

(3) to establish a nomenclature for the new specificities identified by serological techniques on B lymphocytes.

Specificities for HLA-A, HLA-B, and HLA-C loci

The newly upgraded specificities are listed in Table 1. In deciding which specificities should be upgraded, in addition to clarity and reproductibility of definition, general availability of the appropriate antisera was taken into account.

Although the specificities Cw1, Cw2, Cw3, and Cw4 are now considered to be sufficiently well defined to satisfy the qualifications for upgrading to full HLA status, it has been decided not to change the nomenclature, at least for the time being, to avoid any possible confusion with the nomenclature

* This terminology note was prepared by the WHO nomenclature committee on leukocyte antigens. The names of the members of the committee are listed on pages 464-465. The article has also been published in *Zeitschrift für Immunitätsforschung*, 153: 373-379 (1977). A French version of this article will appear in a future issue of the *Bulletin*.

Table 2. New designations for provisional specificities of the HLA-B and HLA-C loci

New	Representative equivalents
HLA-Bw4	w4, 4a
HLA-Bw6	w6, 4b
HLA-Bw44	B12 (not TT*)
HLA-Bw45	TT*
HLA-Bw46	HS, SIN2
HLA-Bw47	407*, MO66, CAS, Bw40C
HLA-Bw48	KSO, JA, Bw40.3
HLA-Bw49	Bw21.1, SL-ET
HLA-Bw50	Bw21.2, ET*
HLA-Bw51	B5.1
HLA-Bw52	B5.2
HLA-Bw53	HR
HLA-Bw54	Bw22j, SAP1
HLA-Cw6	T7

for the complement components C2 and C4, coded for, at least in part, by genes in the HLA region. Steps are being taken to consult with the IUIS Complement Nomenclature Sub-committee as to the symbols to be used for these complement loci.

New provisional designations for specificities of the HLA-B and HLA-C loci are listed in Table 2. These designations conform to the previously established principles—namely, that the specificities of the HLA-A and HLA-B loci are numbered jointly, so that there is no overlap in numbers between them, that numbers are retained for a specificity that may be split (e.g., HLA-A9, split into HLA-Aw23 and HLA-Aw24), and that numbers once used are never reassigned. It is recommended, however, that when both “broad” cross-reacting specificities and “narrow” or subtypic specificities are included in a phenotype designation, the broad specificities may be listed in parentheses at the end of the set of specificities for each locus, e.g., HLA-A1, 26 (10); B27, w50 (w21, w4, w6). The listing of broad specificities in this way, in addition to the narrow subtypic specificities, is optional. When, however, only the broad specificity is identified this is listed in the usual way, e.g., HLA-A1, 10; B27, w21.

HLA-Bw4 (previously w4 or 4a) and HLA-Bw6 (previously w6 or 4b) are now specifically associated with the B locus because of chemical evidence for their presence on the same molecules that carry the other HLA-B locus specificities. These two specificities often help considerably in distinguishing splits in B locus specificities. For example, in the case of HLA-Bw21 splits, HLA-Bw49 (previously Bw21.1 or SL-ET) is HLA-Bw4 associated while

HLA-Bw50 (previously Bw21.2 or ET*) is HLA-Bw6 associated.

In certain cases, e.g., HLA-Bw53 (previously HR), a provisional specificity has been assigned even though all sera also contain antibodies against other specificities, in this case HLA-B5 and/or HLA-Bw35.

HLA-Bw45 (previously TT*) is most frequently found in certain African groups and is, for example, quite rare in European Caucasoid populations. This means that in practice, in European Caucasoids, HLA-B12 individuals are nearly always HLA-Bw44. When, however, sera identifying HLA-Bw45 have been used and an individual has been shown to be negative for this specificity, this person should be designated HLA-Bw44 or HLA-Bw44 (12) and not just HLA-B12.

In some cases it may be helpful to include a broad specificity in the genotype, following the same rules recommended above for the phenotype. For example, in the absence of sera identifying HLA-Bw45 but given typing for Bw4 and Bw6, a genotype HLA-A1, B8(w6)/A2, B12(w4) would clearly indicate that the HLA-A2, B12(w4) haplotype was probably HLA-A2, Bw44.

As is the case for a number of the previously established HLA specificities, certain of the newly designated provisional specificities are found predominantly in particular population groups, as already mentioned for Bw45. For example, HLA-Bw53 (previously HR) is found mainly in Negroes from Africa and America, HLA-Bw54 (previously Bw22J, etc.) and HLA-Bw46 (previously HS, SIN2) in Orientals and HLA-Bw48 (previously KSO, etc.) in Eskimos, American Indians, and possibly other oriental related populations.

The following suggested specificities were discussed, but were considered not yet sufficiently well defined to be assigned a provisional w designation: 9.3, 5.3, 5.4, 14.1, 14.2, 15.1, 15.2, 15A, 17 long, 17 short, 22.1, 22.2, DA30, 35A, 35C, 40.1, 40.2, DB, IM2, BU, T6.

HLA-D specificities

There has been a significant advance in the definition of certain of the HLA-D locus specificities, notably HLA-Dw1, HLA-Dw2, and HLA-Dw3. Nevertheless, the practical difficulties of cell typing do not yet justify the upgrading of any of these specificities to full HLA status. New designations for provisional specificities of the HLA-D locus are given in Table 3. The new specificity HLA-Dw11

Table 3. New designations for provisional specificities of the HLA-D locus

New	Previous or representative equivalent
HLA-Dw7	LD107
HLA-Dw8	LD108
HLA-Dw9	TB9, OH
HLA-Dw10	LD16
HLA-Dw11	LD17

(previously LD17) appears to be more or less included in HLA-Dw7 and may turn out to be a "split" of this latter specificity.

Other suggested specificities discussed but not yet considered ready for provisional w designation, pending further cell exchanges evaluated by appropriate statistical procedures, were RE and the Japanese specificities HO and YT or AW. Further exchanges are also needed before other suggested MLC loci, possibly distinct from HLA-D, can be considered. At the 6th and 7th Workshops on Histocompatibility Testing a group of reference laboratories for cellular typing was established, on an informal basis, and these laboratories are continuing to collaborate in cell exchanges in order to clarify the definition of these and other proposed specificities (4).

Specificities identified by serological techniques on B lymphocytes

The 7th Workshop consolidated a major advance in the definition of the new specificities identified by serological techniques on B lymphocytes, mainly using a microlymphocytotoxicity assay on purified peripheral blood B lymphocytes. These specificities, which appear to be the counterpart of at least some of the so called Ia determinants of the mouse major histocompatibility system, H-2, are in general closely associated with the already defined specificities of the HLA-D locus. In order to reflect this relationship, while at the same time reserving judgement on whether these serologically detected determinants are on the products of the HLA-D locus, it has been decided to use for them the designation DR (for D related), followed, as usual, by the letter w to indicate that the designation is still provisional. This nomenclature for the first seven DRw specificities, using numbers that correspond to the relevant associated Dw specificity, is given in Table 4, together with their 7th Workshop equivalents. The

Table 4. Nomenclature for the new specificities established by serological assays on B lymphocytes

New nomenclature	7th Workshop nomenclature ^a
DRw1	WIA1
DRw2	WIA2
DRw3	WIA3
DRw4	WIA4
DRw5	WIA5
DRw6	WIA6
DRw7	WIA7

^a Other equivalent nomenclatures and further details concerning the definition of these specificities can be found in Bodmer et al. (4).

specificities DRw1, DRw2, DRw3, and DRw7 are clearly defined, each by several sera. DRw4 has been defined in two ways. First, by sera that show some evidence of cross-reaction with DRw5 but do not consistently react with any other specificity; second, by sera that contain activity against DRw4 and DRw7, and so can be used to define DRw4 only in the absence of DRw7, again reflecting cross-reaction, in this case between DRw4 and DRw7. The specificity DRw6 is the least well defined, as the available sera react in addition either with DRw3 and possibly DRw5, or with DRw2 and often also DRw1. These cross-reaction patterns, which seem to be a common feature of the DRw specificities, may reflect the existence of supertypic specificities for, for example, the combinations DRw1, DRw2, and DRw6, or DRw4, DRw5, and possibly DRw7. Allowing for these problems of cross-reaction, the evidence so far is consistent with the hypothesis that these seven specificities are controlled genetically by a single multiple allelic series, as in the case of the HLA-A, B, C, and D loci.

In the 7th Workshop, an effort was made to define an HLA-Dw8 associated specificity (Workshop designation WIA8) but this was considered to be not yet sufficiently well established to be assigned a provisional w designation. There were, in addition, a number of suggestions for other specificities, mainly identified as "tails" in the 7th Workshop sera, and these also need further evaluation before they can be considered for a w designation. Some evidence has been obtained, both before and during the Workshop, for the existence of one or more determinants coded for by a locus in the neighbourhood of HLA-A, but once again further work is needed before this can be considered for a new locus symbol. It is probable that, in due course, serological tests on B

Table 5. Complete listing of recognized HLA specificities ^a

HLA-A	HLA-B	HLA-C	HLA-D	HLA-DR
HLA-A1	HLA-B5	HLA-Bw42	HLA-Dw1	HLA-DRw1
HLA-A2	HLA-B7	HLA-Bw44	HLA-Dw2	HLA-DRw2
HLA-A3	HLA-B8	HLA-Bw45	HLA-Dw3	HLA-DRw3
HLA-A9	HLA-B12	HLA-Bw46	HLA-Dw4	HLA-DRw4
HLA-A10	HLA-B13	HLA-Bw47	HLA-Cw5	HLA-DRw5
HLA-A11	HLA-B14	HLA-Bw48	HLA-Cw6	HLA-DRw6
HLA-Aw19	HLA-B15	HLA-Bw49		HLA-DRw7
HLA-Aw23	HLA-Bw16	HLA-Bw50		
HLA-Aw24	HLA-B17	HLA-Bw51		
HLA-A25	HLA-B18	HLA-Bw52		
HLA-A26	HLA-Bw21	HLA-Bw53	HLA-Dw6	
HLA-A28	HLA-Bw22	HLA-Bw54	HLA-Dw7	
HLA-A29	HLA-B27		HLA-Dw8	
HLA-Aw30	HLA-Bw35		HLA-Dw9	
HLA-Aw31	HLA-B37		HLA-Dw10	
HLA-Aw32	HLA-Bw38		HLA-Dw11	
HLA-Aw33	HLA-Bw39			
HLA-Aw34	HLA-B40			
HLA-Aw36	HLA-Bw41			
HLA-Aw43				
	HLA-Bw4			
	HLA-Bw6			

^a The following specificities arose as clear-cut splits of other specificities:

HLA-A9	into	HLA-Aw23	HLA-Aw24
HLA-A10	into	HLA-A25	HLA-A26
HLA-B5	into	HLA-Bw51	HLA-Bw52
HLA-B12	into	HLA-Bw44	HLA-Bw45
HLA-Bw16	into	HLA-Bw38	HLA-Bw39
HLA-Bw21	into	HLA-Bw49	HLA-Bw5

Historically HLA-Aw19 has included HLA-A29, HLA-Aw30, HLA-Aw31, HLA-Aw32, and HLA-Aw33.

lymphocytes and other techniques including, for example, the primed lymphocyte test (PLT) and cell-mediated lymphocytotoxicity (CML) may define other loci in and outside the HLA region. Though evidence has been obtained that suggests a relatively close relation between determinants identified using the PLT test and the DRw and similar specificities, the results of the 7th Workshop exchange did not warrant the designation of any separate nomenclature for these.

The committee adheres to the view that it should confine its attention to the cell surface determinants, identified by serological and cellular techniques, that are coded for by genes in the HLA region. This does not exclude the possibility that it may in the future have to broaden its horizon beyond the HLA region. However, the committee reaffirms its recommendation that the pre-emption of formal symbols, such as HLB, HL-B or HLA-E, that are clearly related to the symbols used in the nomenclature for factors of the HLA system, is to be strongly discouraged before their use has been considered by the committee.

The members of the committee accept that their laboratories should play a major role in the ex-

changes of sera, cells, and information that are needed to continue to clarify the definition of new and proposed factors of the HLA system. This cooperation provides a network of reference laboratories that can, together with the workshops, continue to aid the clear development of knowledge of the HLA system.

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REFERENCES

1. *Bulletin of the World Health Organization*, **39**: 483 (1968).
 2. *Bulletin of the World Health Organization*, **47**: 659 (1972).
 3. *Bulletin of the World Health Organization*, **52**: 261 (1975).
 4. BODMER, W. F. ET AL., ED. *Histocompatibility testing*. Copenhagen, Munksgaard, 1977.
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