Nomenclature for factors of the HLA system*

A Nomenclature Committee composed of geneticists and immunologists, including specialists in tissue typing, has met after each of the Histocompatibility Workshops beginning with the Third Workshop in 1967. The Committee, in part under the auspices of the World Health Organization and the International Union of Immunological Societies (WHO/IUIS), met after the Sixth Workshop in Aarhus in July 1975. The expanding knowledge of the genetics of the major histocompatibility system of man has necessitated a revision of the terminology for the HLA region following the principles established in previous reports. This has been done with as few changes as possible.

It has been realized for a number of years that in man there is a major histocompatibility system of great complexity, homologous to those of other mammalian species and composed of a series of many closely-linked genes. The original serologically-defined specificities of the HLA system were assigned to two separate series (first or LA, and second or FOUR) corresponding to two linked loci with multiple alleles. These loci have been assigned to chromosome 6, both by family studies and by genetic analysis with somatic cell hybrids. Recent studies, especially in mouse and man, have shown that the genetic region identified by these two loci also contains many other genes controlling cell surface determinants, immune reponse differences, some components of the complement system and, perhaps, other related functions. The purpose of the revised nomenclature is to take account of this increasing complexity.

The genetic region encompassing this large series of interrelated loci will be called HLA (the hyphen previously used in the designation of the HLA system is being dropped in order to minimize the increasing number of symbols needed to define loci and specificities belonging to the system). Genetic loci belonging to the system will be designated by one or more letters following the HLA. Individual alleles of each locus, and the corresponding specificities, will be designated by numbers following the locus symbols. Provisionally identified specificities will, as before, carry the additional letter W(w), which will now be inserted between the locus letter(s) and the allele and specificity number. Although many computer outputs contain only capital letters, nevertheless it is suggested that in writing and printing a lower case " w " should be used.

The general notational scheme is therefore as follows:

HLA: region or system designation.

A, B, C, D, etc.: locus symbols.

W (w): symbol to indicate a provisional specificity (may later be dropped when specificity is confirmed).

1, 2, etc.: number identifying specificities belonging to each locus.

Detailed examples of this system of notation are given later.

The decision as to whether a locus belongs to the HLA system will, as discussed in previous reports, be based at least on genetic mapping data, on evidence as to function and chemical structure, and on population data showing evidence of significant population associations (linkage disequilibrium). By these criteria, for example, a human analogue of the mouse T1a locus would most probably be assigned to the HLA system. The loci controlling complement components C2, C4, and properdin factor B (GBG, Bf, etc.), as well as those controlling the Chido and Rogers blood groups, should probably also be assigned to HLA. In this report, however, we shall confine our attention to the serologically-defined determinants found mainly on lymphocytes, other nucleated cells, and also platelets, and to the determinants recently identified by MLC-typing (mixed lymphocyte cultures).

The loci previously called LA (or first) and FOUR (or second) will now be designated by the letters A and B, respectively. The complete locus symbols will therefore be HLA-A for the LA (or first), and HLA-

* This Terminology Note was drafted by the signatories listed on page 265. A French version will be published in a future issue of the *Bulletin*.

B for the FOUR (or second) loci. For historical reasons the specificities determined by the alleles of these two loci are numbered jointly, so that apart from W5 and W10 (see below), there is no overlap in numbers between them. For example, specificities 1, 2, 3, 9, 10, 11, etc. belong to the HLA-A locus while 5, 7, 8, 12, 13, etc. belong to the HLA-B locus. This joint numbering scheme will be continued for these first two loci, and in local use the prefixes A and B may be optional. For other loci (C, D, etc.) the numbering of specificities will start in sequence from 1, separately for each locus, so that the prefix locus letter will be an essential part of the notation for a specificity. It is expected that, in most cases, a specificity will first receive a provisional w designation, but may later be upgraded by omitting the w, while keeping the same number.

The locus designated by the prefix C corresponds to that previously known as the AJ or third locus, and the locus designated D corresponds to what has variously been called MLR-S1, LD-1, MLC-1, etc.

The Committee recognized that many new specificities are being detected on lymphoid subpopulations such as B cells, T cells, lymphoblastoid lines, and chronic lymphatic leukaemia cells. Some of these specificities can also be detected on, for example, macrophages, endothelial cells, and sperm. It is probable that more than one locus is represented, as is the case for the corresponding specificities in the mouse, and as may also prove to be the case for lymphocyte-stimulating activities now provisionally assigned to locus D. Since the knowledge concerning these newer serological specificities is very recent and incomplete, it was felt that the assignment of one or more loci to them was premature.

An approach will be made to the Committee, at an appropriate future date, concerning the symbols to be used for the loci in the HLA region controlling or regulating some complement components.

The Committee considered the status of the existing W specificities and agreed that a number of them could now be upgraded from their provisional status. In considering the state of definition of a specificity, the previous criteria were somewhat modified. A specificity formerly designated W was upgraded to full HLA status provided it could be clearly and reproducibly recognized by several generally available antisera, which were represented at one or more workshops. The antigens so considered had all been tested for segregation in informative families and, generally, for their consistent behaviour in different populations.[a] Absorptions are, in general, required but it was felt that absorption had less significance than had previously been thought

Table 1. New designations for specificities of the HLA-A and HLA-B loci

New HLA nomenclature	Old nomenclature	Representative equivalents where applicable
HLA-B14	W14	
HLA-B18	W18	
HLA-B27	W27	
HLA-A28	W28	
HLA-A29	W29	
HLA-Aw33	W19.6	including Fe55, 10.4, Bar 3 Malay 1
HLA-Aw34 [a]		Malay 2, HL-A10-3, F26
HLA-Bw35	W5	
HLA-Aw36 [a]		Mo*, LT
HLA-Bw37		TY
HLA-Bw38	W16.1	W16,W4, Da31
HLA-Bw39	W16.2	W16,W6, W16,382
HLA-Bw40	W10	
HLA-Bw41		Sabell, LK, Da34
HLA-Bw42 [a]		MWA
HLA-Aw43 [a]		BK

[a] Some of the new specificities are most frequently identified in certain population groups. Examples are Aw36, Bw42, and Aw43, which are most frequently found in certain African groups. HLA-Aw34 (HLA-10 related antigen) is frequently observed in some Orientals and in some Blacks from Africa and America.

Table 2. New designations for specificities of the HLA-C and HLA-D loci [a]

New HLA-C nomenclature	Representative equivalents	New HLA-D nomenclature
HLA-Cw1	T1-AJ	HLA-Dw1
HLA-Cw2	T2-Sa532	HLA-Dw2
HLA-Cw3	T3-UPS	HLA-Dw3
HLA-Cw4	T4-RH315	HLA-Dw4
HLA-Cw5	T5	HLA-Dw5
		HLA-Dw6

[a] For a more complete listing of Dw equivalents see Table 4.

[a] *Bulletin of the World Health Organization*, 47: 659-662 (1972).

Table 3. Complete listing of recognized HLA specificities [a]

New	Previous [b]	New	Previous	New	Previous	New	Previous
HLA-A1	HL-A1	HLA-B5	HL-A5	HLA-Cw1	T1	HLA-Dw1	LD 101
HLA-A2	HL-A2	HLA-B7	HL-A7	HLA-Cw2	T2	HLA-Dw2	LD 102
HLA-A3	HL-A3	HLA-B8	HL-A8	HLA-Cw3	T3	HLA-Dw3	LD 103
HLA-A9	HL-A9	HLA-B12	HL-A12	HLA-Cw4	T4	HLA-Dw4	LD 104
HLA-A10	HL-A10	HLA-B13	HL-A13	HLA-Cw5	T5	HLA-Dw5	LD 105
HLA-A11	HL-A11	HLA-B14	W14			HLA-Dw6	LD 106
HLA-A28	W28	HLA-B18	W18				
HLA-A29	W29	HLA-B27	W27				
HLA-Aw19	Li [c]	HLA-Bw15	W15				
HLA-Aw23	W23	HLA-Bw16	W16				
HLA-Aw24	W24	HLA-Bw17	W17				
HLA-Aw25	W25	HLA-Bw21	W21				
HLA-Aw26	W26	HLA-Bw22	W22				
HLA-Aw30	W30	HLA-Bw35	W5				
HLA-Aw31	W31	HLA-Bw37	TY				
HLA-Aw32	W32	HLA-Bw38	W16.1				
HLA-Aw33	W19.6	HLA-Bw39	W16.2				
HLA-Aw34	Malay 2	HLA-Bw40	W10				
HLA-Aw36	Mo*	HLA-Bw41	Sabell				
HLA-Aw43	BK	HLA-Bw42	MWA				

[a] The previously reserved specificities W4 (4a) and W6 (4b) remain w4 and w6. These specificities are closely associated with the B locus.

[b] For a more comprehensive listing of equivalents see Table 1 and the ' table of equivalent nomenclature ' in : Dausset, J. & Colombani J., ed. Histocompatibility testing. Copenhagen, Munksgaard, 1972, p. 7.

[c] HLA-Aw19 includes at least HLA-A29, Aw30, Aw31, Aw32, Aw33, and Aw34 (?).

because of the quantitative difficulties associated with varying degrees of cross-reactivity. Absorption is, however, still considered important and especially useful in the preliminary identification of new specificities. To this aim co-capping and stripping are other important serological tools. The upgraded specificities and newly designated w specificities, together with their previous equivalents, are listed in Table 1.

The new provisional Cw and Dw specificities, together with their previous equivalents, are given in Table 2.

The specificities W5 and W10 have, for historical reasons, been the only designations that overlap other numbered specificities (HLA-B5 and HLA-A10). In order to correct this anomaly, it is proposed to renumber the W5 specificity Bw35 and the W10 specificity Bw40, as indicated in Table 1. The ' local ' HLA-B specificities, TT* (HLA-B12 related), 407*, KSO (=JA), HR, and HS (=SIN 2) are still under consideration for upgrading.

A complete listing of all recognized HLA specificities is given in Table 3, together with the most common of the previously used symbols. A more comprehensive list of equivalents for the HLA-D specificities is given in Table 4.

Many additional specificities were considered as candidates for w classification. Those not included in Tables 1 and 2 were withheld pending further clarification by WHO collaborating laboratories. The specificities HLA-Aw32, Aw33, Bw17, Bw21, B5 (previously HL-A5), Bw35, HR, Bw38, Bw39, TT *,

Table 4. List of equivalent HLA-D antigen designations

Nomenclature		Laboratory No.[a]												
WHO	workshop	1	2	3	6	7	8	9	11	12	13	14	15
Dw1	LD 101	MLR-S W5a			Theis Lad27a Fes 1	LD-W5a	Tasz	TB1	LD-W5a	LD-W5a	'J'	PF	LD-XVII
Dw2	LD 102	MLR-S 7a	LD-7a	LD-7a	Fes 2	LD-7a		TB3	LD-7a	LD-7a	'S'	PI(BA)	LD-V
Dw3	LD 103	MLR-S 8a	LD-8a LD-8b	LD-8ab		LD-8a	Plock	TB4	LD-8a	LD-8a		SR	LD-XI
Dw4	LD 104		R LD-12a	LD-12a LD-W15a		LD-12a		TB5	LD-W15a	LD-W15a	'L'		LD-XVIII
Dw5	LD 105			SFN1				TB2	LD-'W16a'	Sa[1]			LD-IV
Dw6	LD 106					LD-W15a	Krej	TB6	LD-pm	Pr			LD-XIV
	LD 107		LD-12b		Fes 3				LD-12a	LD-12a			LD-XII
	LD 108								LD-ae	LD-W10a			

[a] The investigators belonging to the individual laboratories will appear in the list of LD laboratories and in the LD-reports from these laboratories published in: Kissmeyer-Nielsen, F., ed. Histocompatibility testing. Copenhagen, Munksgaard, 1975.

407 *, and KSO (JA) are under consideration for upgrading or further clarification. For these purposes the collaborating laboratories will solicit additional antisera from other investigators and will exchange sera and, where practicable, informative cells with other groups. Absorption, family, and population studies will be carried out, following the principles set out in this and previous reports, and revision of status will then be further considered by the Committee. A list of the WHO collaborating laboratories is given in the Annex.

Some typical examples of the usage of the new terminology will now be given. An individual carrying the specificities A1, A3, B7, B8 might, for example, also carry the specificities Cw1, Cw2. The phenotype would be given as HLA-A1, 3; B7, 8; Cw1, w2. Note that in writing the phenotype, serological specificities controlled by the same locus are separated by commas, while products of different loci are separated by semicolons. This avoids repetition of the locus symbols and also makes it easy to incorporate cross-reacting and subtypic specificities (e.g., HLA-A9, 10, w23, w25; Bw16, w37; C . . .). The genotype would be written in terms of the two haplotypes as HLA-A1, B8, Cw1/A3, B7, Cw2. Other possible phenotypes would, for example, be HLA-A1, w32; Bw22, w35; Cw1, w3, or HLA-A1, 28; B7, w37; Cw1; Dw2. The presence of only a single specificity for a locus implies a phenotypic blank with respect to the specificities being tested for. A blank in a genotype, established by a family study, could be written, for example, as HLA-A1, Bw35, C–, Dw2/A28, B7, Cw1, D–. When w4 (4a) and w6 (4b) are designated in a pheno- or genotype, they can be inserted after the B locus specificities, e.g., HLA-Ax, y; B7, 12, w4, w6; Cx, y. Following a convention widely accepted in genetics, genetic symbols such as for loci, alleles, haplotypes, or genotypes, should be italicized in print and underlined in manuscripts and typed scripts, while antigens, serological specificities, etc. should be written and printed in normal type (e.g., A1 is the antigen; *A1* or A1 is the corresponding allele). The loci in the haplotype are written in alphabetical order and so do not represent the relative map position on the chromosome.

There may often be no need to include the system prefix, HLA, when it is clear from the context that loci of this system are being referred to.

In its revision of nomenclature, the Committee considered and unanimously rejected various alternative suggestions, including the possibility of desig-

nating the lymphocyte activating determinants and lymphocyte subclass specificities HL-B, HL-C, etc. Attention is drawn to a previous statement on this point, to the effect that the major designations be reserved for other genetic systems not closely linked to or part of the HLA region. The pre-emption of formal symbols such as HLB (or HL-B), HLA-E, etc. before their use has been formally considered by this nomenclature committee, is to be strongly discouraged as being detrimental to a clear development of a systematic classification.

We realize that no system of notation can be guaranteed to cope with all future developments. In particular if, as seems likely, the D-locus is split, its specificities may have to be reassigned. We do, however, believe that the system proposed here has considerable flexibility and can be adopted with minimal changes to present usage.

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ACKNOWLEDGEMENTS

The contributions of Dr Julia Bodmer, Dr Sergio Curtoni, Dr Alberto Piazza, and Dr Erik Thorsby to this report are gratefully acknowledged.

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