

Terminology Terminologie

Nomenclature for factors of the HLA system, 1984*

This article presents the decisions of the nomenclature committee on leukocyte antigens, which met in Vienna on 16-17 May 1984.

The HLA nomenclature committee met under the auspices of the World Health Organization, after the Ninth International Histocompatibility Testing Workshop which was held in Munich and Vienna on 6-15 May 1984, to consider revisions and additions to the nomenclature of factors identified by serological and cellular typing following the principles established successively in previous reports (1-6). The nomenclature for the variants of the complement components controlled by genes of the HLA region was not considered, as it was assumed that this was the responsibility of those with a special interest in complement (see reference 7). Special attention was given to establishing a revised system of nomenclature for the products (sometimes called class II) of what can now be called the HLA-D region, based on the recent advances in our understanding of the biochemistry and genetics of these products.

The decision to upgrade a specificity, namely to drop its "w" designation, took into account the correlation in the overall workshop data between the local laboratory assignment of a specificity and that arrived at by the central computer analysis. A correlation coefficient of around 0.95 or higher, together with general availability of appropriate antisera, was taken as a sufficient indication of adequate clarity of definition of a specificity to drop the "w" designation. This criterion was applied equally to broader and narrower specificities even though, in some cases, the splits of the broader specificity were not so well defined. This is, for example, still the case for HLA-B5 with its splits B51 and Bw52. The retention of a "w" in the designation

remains an indication that the specificity, though clearly identified, may not always be easily defined.

HLA-A, HLA-B, and HLA-C specificities

As before, the HLA-A and HLA-B specificities are numbered jointly with non-overlapping numbers. The "w" designation is retained for all HLA-C specificities to avoid confusion with the nomenclature for complement components.

Newly upgraded HLA-A and HLA-B specificities are listed in Table 1. In addition to Cw1, Cw2, Cw3, Cw4 and Cw5, Cw6 approaches the clarity of definition that would be required for dropping the "w" designation. However, Cw5 remains slightly more difficult to define than Cw1, Cw2, Cw3 or Cw4.

New provisional designations for HLA-A and HLA-B specificities are listed in Tables 2 and 3 respectively. Aw66 (previously LN) is effectively another split of A10 and cannot so far be defined serologically in the presence of A26. Aw69 (previously A2/28) is a split of A28 that is most clearly defined by monoclonal antibodies with reactivity only against A2 and Aw69, and cannot so far be defined serologically in the presence of A2. This is the first example of an officially recognized specificity identified by a monoclonal antibody. Given the potential exquisite specificity of monoclonal antibodies, criteria for the designation of new specificities identified by them need careful consideration. Aw69 has been designated because at least two monoclonal antibodies agree in defining a new specificity that is clearly distinct from any previously identified specificity. Aw68 is defined as the split of A28 that is complementary to Aw69. Since Bw71 (previously Bu) and Bw72 (previously SV) cannot always be distinguished serologically from each other, it was also necessary to designate the broad specificity Bw70 (previously

* A French translation of this article appears on pages 407-413. The names of the members of the committee that prepared this note are given on pages 402 and 405. Requests for reprints should be sent to Chief, Immunology, World Health Organization, 1211 Geneva 27, Switzerland.

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

New	Previous equivalents
A23	Aw23
A24	Aw24
A30	Aw30
A31	Aw31
A32	Aw32
B16	Bw16
B21	Bw21
B35	Bw35
B38	Bw38
B39	Bw39
B44	Bw44
B45	Bw45
B49	Bw49
B51	Bw51

Table 2. New provisional designations of HLA-A specificities

New	Previous equivalents
Aw66	LN
Aw68	A28 and negative to A2/28
Aw69	A2/28

Table 3. New provisional designations for HLA-B specificities

New	Previous equivalents
Bw64	B14 1, (8w63)
Bw65	B14 2, (8w62)
Bw67	SN-2, Te90, (8w57), Te75
Bw70	Bu + SV, K5, Da(6), (8w59)
Bw71	Bu
Bw72	SV
Bw73	KA, IEH

Bu + SV, K5 or Da(6)).

Other suggested HLA-A or HLA-B specificities discussed, but not yet considered to be sufficiently well defined to merit official provisional designation, included 9.3, Th (a possible further split of Aw19 in negroid populations), 19bac, 33.1, 33.2, St16 (a possible further split of B39), 15.3 and Te74 (another B15

split sometimes referred to as 8w66, an informal designation that should be avoided to prevent any possible confusion with Aw66). Special attention clearly needs to be given to clarification of the many possible further splits of B15, seen especially in oriental populations.

Individual workshop sera suggested a new specificity that may fill part of the HLA-C blank, and a split of Cw3. Other sera suggested splits of Cw7. However, none of these suggestions were considered to be sufficiently well founded to merit an official provisional designation. The combination of Cw1 and Cw3, seen in association with haplotypes containing Bw46, was not given a separate designation as it is not yet clear whether this is simply a reflection of gene duplication (in whole or in part) or truly represents a novel serological specificity.

The HLA-D region

Biochemical and molecular genetical analyses of the products and genes associated with the HLA-Dw and HLA-DR(w) specificities have led to a considerable advance in our understanding of the HLA-D region and its products. It is now clear that there are at least three well-defined subsets of products, which until now have been informally designated as DR, DC (MB or DS) and SB. Each product consists of a non-covalently associated combination of an α - and a β -chain. The α and β chains are substantially different from each other, and there is evidence for at least six α chain genes and seven β chain genes all in the HLA region. These genes, for the most part, appear to be arranged in subsets corresponding to the three subsets of products, where α and β chain genes within a subset are significantly more similar to each other than they are to the genes of one of the other subsets. While present knowledge concerning the genes of the HLA-D region is not yet adequate to give them each an official designation, it was decided that the division into three subsets of products is sufficiently well established to merit an official designation and that this could be done without prejudicing future decisions on nomenclature for the specificities and genes of the HLA-D region. The chosen designations are HLA-DR, HLA-DQ (previously DC, etc.), and HLA-DP (previously SB). Current evidence suggests one α and two or three β chain genes for HLA-DR, and two α and two β chains each for HLA-DQ and HLA-DP. It is anticipated that when eventually gene names are officially designated they will consist of HLA-DR, HLA-DQ, HLA-DP, followed by a combination of numbers and letters (A for an α -chain gene and B for a β -chain gene) that uniquely defines each gene. The HLA-D region is the counterpart of the I-region of the mouse H-2 system, whose determinants are sometimes called Ia, with I-A

corresponding to DQ, and I-E to DR.

The serologically defined specificities of the HLA-D region can be associated predominantly with either the HLA-DR or HLA-DQ sets of products, while the different HLA-DP products are so far only defined using the primed lymphocyte test (or PLT). Certain monomorphic monoclonal antibodies can, however, clearly distinguish between these three sets of products.

The HLA-Dw specificities, defined by the mixed lymphocyte culture (or MLC) test, cannot yet be clearly associated with one or other of the three subsets of products, though it seems likely that they mostly involve HLA-DR. Where new specificities are clearly identified as being associated predominantly with one or other of the subsets of HLA-D products, we have followed previous practice in assigning to them the designation HLA-DR, HLA-DQ or HLA-DP (followed by "w" to indicate that the designation is provisional) and appropriate numbers, usually in sequence. The designation HLA-Dw, with no further indication of subdivisions, is retained for the MLC-defined specificities.

HLA-DR specificities

The previously defined HLA-DR1, DR2, DR3, DR4, DR5, DRw6, DR7, DRw8, DRw9, and DRw10 specificities are all clearly associated with the HLA-DR products. They therefore retain their previous designations, since it was decided that none of DRw6, DRw8, DRw9 or DRw10 deserved to be upgraded to full HLA status. Amongst HLA-DR specificities with full HLA status, DR5 remains the most difficult to define.

New provisional designations for HLA-DR specificities are given in Table 4. DRw11 (previously LB5) and DRw12 (previously LB5x8, etc.) are splits of DR5, while DRw13 (previously 6.6, 6.1, 6Z) and DRw14 (previously 6.3, 6.9, 6X, 901) are splits of DRw6.

DRw52 (previously MT2) and DRw53 (previously MT3) were originally identified in the 7th and 8th Workshops as apparently cross-reacting specificities involving DR3, DR5, DRw6 and DRw8 for DRw52, and DR4, DR7 and DRw9 for DRw53. Following the 8th Workshop, it was suggested that these two specificities might be on molecules from a different locus (sometimes also referred to as BR) to that controlling the then designated HLA-DR specificities, or possibly on molecules from both the then assumed HLA-DR locus and another locus, and this remains true. But it is now clear that all such molecules must be members of the HLA-DR subset. High numbers were chosen for these two broad, operationally supertypic, specificities to separate them clearly from the other, narrower HLA-DR

Table 4. New provisional designations for HLA-DR specificities

New	Previous equivalents
DRw11	LB5
DRw12	LB5x8, DR5 short, FT23
DRw13	6.6, 6.1, 6Z
DRw14	6.9, 6.3, 6X, 901
DRw52	MT2
DRw53	MT3

Table 5. New provisional designations of HLA-DQ specificities

New	Previous equivalents
DQw1	DC1, MB1, MT1, LB-E12
DQw2	MB2, DC3, Te24, LB-E17
DQw3	MB3, MT4, DC4, TB21

specificities. DRw6, in particular, seems operationally to be completely included in DRw52 (previously MT2).

Other suggested HLA-DR specificities that were discussed, but not yet considered to be sufficiently well defined to merit official provisional designation, included 4.1, 4.2, 4.3, and DR2 splits.

HLA-DQ specificities

New provisional HLA-DQ specificities are listed in Table 5. As in the case of DRw52 (previously MT2) and DRw53 (previously MT3), DQw1 (previously DC1, MB1, MT1, LB-E12), DQw2 (previously MB2, DC3, Te24, LB-E17), and DQw3 (previously MB3, MT4, DC4, TB21) were originally identified in the 7th and 8th Workshops as apparently cross-reacting specificities including DR1, DR2, DRw6 and DRw10 for DQw1, DR3 and DR7 for DQw2, and DR4 and DR5 for DQw3. These were also suggested at the time of the 8th Workshop to be on different locus products from the HLA-DR specificities. Subsequent studies, in this case, have clearly associated these specificities with the HLA-DQ (previously DC, etc.) products. TA10 and LB-E13 were discussed as possible HLA-DQ specificities, apparently splitting DQw3, but it was felt that their relationship with HLA-DQ products required some further independent confirmation, and so they were not assigned official provisional designations.

The fact that DQw1 (previously DC1, etc.) and DRw6 are on different sets of products clearly

Table 6. New provisional designations for HLA-DP specificities

New	Previous equivalents
DPw1	SB1, PL3A
DPw2	SB2
DPw3	SB3
DPw4	SB4, PL3B
DPw5	SB5
DPw6	SB6

indicates that DQw1 does not contribute to the definition of DRw6. The strong population associations between these and other analogous combinations of specificities can now be seen clearly to be due to strong linkage disequilibrium between alleles at very closely linked loci coding for DR and DQ products.

HLA-DP specificities

New provisional HLA-DP specificities, as defined by PLT typing, are listed in Table 6.

Table 7. New provisional designations for HLA-Dw specificities

New	Previous equivalents
Dw13	DB3
Dw14	LD40
Dw15	DYT, YT
Dw16	DB8, B8
Dw17	7A, (Dw7A)
Dw18	6A, (Dw6A)
Dw19	6B, (Dw6B)

Table 8. Dw and DR relationships

Dw specificities	Associated DR specificities
Dw1	DR1
Dw2, Dw12	DR2
Dw3	DR3
Dw4, Dw10, Dw13, Dw14, Dw15	DR4
Dw5	DRw11 (5)
Dw6, Dw18, Dw19	DRw13 (w6)
Dw9, Dw16	DRw14 (w6)
Dw7, Dw11, Dw17	DR7
Dw8	DRw8

HLA-Dw specificities

HLA-Dw1, Dw2 and Dw3 now approach the clarity of definition by MLC typing that would justify dropping their "w" designation. However, in order to distinguish the MLC-identified specificities from those clearly assigned to one of the HLA-D region products it was decided, at least for the time being, to use the prefix Dw for all the MLC-identified specificities, however well defined they are.

New provisional designations for HLA-Dw specificities are listed in Table 7. Dw13 (previously DB3), Dw14 (previously LD40), and Dw15 (previously DYT, found predominantly in oriental populations), together with Dw4 and Dw10, are all associated with the serological specificity DR4. Dw2 and Dw12 have similarly previously been associated with DR2. Dw17 (previously 7A) is the complementary split of Dw7 to Dw11, while Dw18 (previously 6A) and Dw19 (previously 6B) are splits of Dw6, which is in turn associated with the serological specificity DRw13, one of the splits of DRw6. The other split of DRw6, DRw14, is associated with Dw9 and Dw16. These multiple relationships between Dw and DR specificities, further confounded by patterns of association with DQ specificities that are probably due to linkage disequilibrium between alleles at DR and DQ loci, emphasize again that it is no longer possible to maintain any relationship between the numbering of Dw and DR specificities. A list of the known relationships between officially designated Dw and DR specificities is given in Table 8.

Other specificities not officially designated included DB6 (originally defined by the cell Herluf), DB9, and a split of Dw8, informally called 8.2, which appears to occur especially in Eskimo and American-Indian populations. These specificities, probably for technical reasons, were not well defined in the final workshop analysis.

A complete listing of the recognized HLA specificities is given in Table 9. Further background to the basis for the decisions reported here can be found in *Histocompatibility testing 1984* (8).

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Table 9. Complete listing of recognized HLA specificities

HLA-A	HLA-B	HLA-C	HLA-D	HLA-DR	HLA-DQ	HLA-DP
A1	B5	Cw1	Dw1	DR1	DQw1	DPw1
A2	B7	Cw2	Dw2	DR2	DQw2	DPw2
A3	B8	Cw3	Dw3	DR3	DQw3	DPw3
A9	B12	Cw4	Dw4	DR4		DPw4
A10	B13	Cw5	Dw5	DR5		DPw5
A11	B14	Cw6	Dw6	DRw6		DPw6
Aw19	B15	Cw7	Dw7	DR7		
A23(9) ^a	B16	Cw8	Dw8	DRw8		
A24(9)	B17		Dw9	DRw9		
A25(10)	B18		Dw10	DRw10		
A26(10)	B21		Dw11(w7) ^a	DRw11(5) ^a		
A28	Bw22		Dw12	DRw12(5)		
A29(w19)	B27		Dw13	DRw13(w6)		
A30(w19)	B35		Dw14	DRw14(w6)		
A31(w19)	B37		Dw15			
A32(w19)	B38(16) ^a		Dw16	DRw52 ^c		
Aw33(w19)	B39(16)		Dw17(w7)	DRw53 ^c		
Aw34(10)	B40		Dw18(w6)			
Aw36	Bw41		Dw19(w6)			
Aw43	Bw42					
Aw66(10)	B44(12)					
Aw68(28)	B45(12)					
Aw69(28)	Bw46					
	Bw47					
	Bw48					
	Bw49(21)					
	Bw50(21)					
	B51(6)					
	Bw52(6)					
	Bw53					
	Bw54(w22)					
	Bw55(w22)					
	Bw56(w22)					
	Bw57(17)					
	Bw58(17)					
	Bw59					
	Bw60(40)					
	Bw61(40)					
	Bw62(15)					
	Bw63(15)					
	Bw64(14)					
	Bw65(14)					
	Bw67					
	Bw70					
	Bw71(w70)					
	Bw72(w70)					
	Bw73					
	Bw4 ^b					
	Bw6 ^b					

(Table 9: continued on next page)

Table 9: *continued*

^a The listing of broad specificities in parentheses after a narrow specificity, e.g., HLA-A23(9), is optional. The following is a listing of those specificities which arose as clear-cut splits of other specificities:

<i>Original broad specificities</i>	<i>Splits</i>
A9	A23, A24
A10	A25, A26, Aw34, Aw66
Aw19	A29, A30, A31, A32, Aw33
A28	Aw68, Aw69
B5	B51, Bw52
B12	B44, B45
B14	Bw64, Bw65
B15	Bw62, Bw63
B16	B38, B39
B17	Bw57, Bw58
B21	B49, Bw50
Bw22	Bw54, Bw55, Bw56
B40	Bw60, Bw61
Bw70	Bw71, Bw72
DR5	DRw11, DRw12
DRw6	DRw13, DRw14
Dw6	Dw18, Dw19
Dw7	Dw11, Dw17

^b The following are the generally agreed inclusions of HLA-B specificities into Bw4 and Bw6.

Bw4: B5, B13, B17, B27, B37, B38(16), B44(12), Bw47, B49(21), B51(15), Bw52(5), Bw53, Bw57(17), Bw58(17), Bw59, Bw63(15)
 Bw6: B7, B8, B14, B18, Bw22, B35, B38(16), B40, Bw41, Bw42, B45(12), Bw46, Bw48, Bw50(21), Bw54(w22), Bw55(w22), Bw56(w22), Bw60(40), Bw61(40), Bw62(15), Bw64(14), Bw67, Bw70, Bw71(w70), Bw72(w70), Bw73.

^c The following specificities are generally agreed to be associated with DRw52 and DRw53:

DRw52: DR3, DR5, DRw6, DRw8, DRw11(5), DRw12(5), DRw13(w6), DRw14(w6)
 DRw53: DR4, DR7, DRw9.

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