

# Blood group terminology 2004: from the International Society of Blood Transfusion committee on terminology for red cell surface antigens

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### Introduction

Human blood groups were discovered over 100 years ago. During the course of the 20th century, a variety of different styles of terminology has been used to denote them. The International Society of Blood Transfusion (ISBT) established a Working Party in 1980 to devise a genetically based numerical terminology for red cell surface antigens. In 1990, the Work-

ing Party published a monograph describing a numerical terminology for 242 red cell antigens [1]. Another monograph listing 254 antigens was published in 1995 [2] and four brief updates have followed [3–6]. In the 9 years since the 1995 report, many amendments to the classification have been necessary: 30 new antigens have been identified and six new systems created. Since 1995, the genes for nine blood group systems have been identified, so that sequenced genes for all 29 systems are now available. All blood group system genes have been located on a specific region of a chromosome (Table 1). The current classification can be found at [www.iccbb.com/ppage107.htm](http://www.iccbb.com/ppage107.htm).

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**Table 1** The blood group systems, the genes that encode them, their chromosomal locations, and associated CD numbers

| No. | System name        | System symbol | Gene name(s) <sup>a</sup> | Chromosomal location | CD numbers        | Refs    |
|-----|--------------------|---------------|---------------------------|----------------------|-------------------|---------|
| 001 | ABO                | ABO           | <i>ABO</i>                | 9q34.2               |                   |         |
| 002 | MNS                | MNS           | <i>GYPA, GYPB, GYPE</i>   | 4q31.21              | CD235             |         |
| 003 | P                  | P1            |                           | 22q11.2–qter         |                   |         |
| 004 | Rh                 | RH            | <i>RHD, RHCE</i>          | 1p36.11              | CD240             |         |
| 005 | Lutheran           | LU            | <i>LU</i>                 | 19q13.32             | CD239             |         |
| 006 | Kell               | KEL           | <i>KEL</i>                | 7q34                 | CD238             |         |
| 007 | Lewis              | LE            | <i>FUT3</i>               | 19p13.3              |                   |         |
| 008 | Duffy              | FY            | <i>FY</i>                 | 1q23.2               | CD234             |         |
| 009 | Kidd               | JK            | <i>SLC14A1</i>            | 18q12.3              |                   | [7,8]   |
| 010 | Diego              | DI            | <i>SLC4A1</i>             | 17q21.31             | CD233             |         |
| 011 | Yt                 | YT            | <i>ACHE</i>               | 7q22.1               |                   |         |
| 012 | Xg                 | XG            | <i>XG, MIC2</i>           | Xp22.33, Yp11.3      | CD99 <sup>b</sup> |         |
| 013 | Scianna            | SC            | <i>ERMAP</i>              | 1p34.2               |                   | [9]     |
| 014 | Dombrock           | DO            | <i>DO</i>                 | 12p12.3              |                   | [10,11] |
| 015 | Colton             | CO            | <i>AQP1</i>               | 7p14.3               |                   |         |
| 016 | Landsteiner-Wiener | LW            | <i>ICAM4</i>              | 19p13.2              | CD242             |         |
| 017 | Chido/Rodgers      | CH/RG         | <i>C4A, C4B</i>           | 6p21.3               |                   |         |
| 018 | H                  | H             | <i>FUT1</i>               | 19q13.33             | CD173             |         |
| 019 | Kx                 | XK            | <i>XK</i>                 | Xp21.1               |                   |         |
| 020 | Gerbich            | GE            | <i>GYPE</i>               | 2q14.3               | CD236             |         |
| 021 | Cromer             | CROM          | <i>DAF</i>                | 1q32.2               | CD55              |         |
| 022 | Knops              | KN            | <i>CR1</i>                | 1q32.2               | CD35              |         |
| 023 | Indian             | IN            | <i>CD44</i>               | 11p13                | CD44              |         |
| 024 | Ok                 | OK            | <i>BSG</i>                | 19p13.3              | CD147             | [12]    |
| 025 | Raph               | RAPH          | <i>CD151</i>              | 11p15.5              | CD151             | [13–15] |
| 026 | John Milton Hagen  | JMH           | <i>SEMA7A</i>             | 15q24.1              | CD108             | [16,17] |
| 027 | I                  | I             | <i>GCNT2</i>              | 6p24.2               |                   | [18,19] |
| 028 | Globoside          | GLOB          | <i>B3GALT3</i>            | 3q26.1               |                   | [20,21] |
| 029 | Gill               | GIL           | <i>AQP3</i>               | 9p13.3               |                   | [22,23] |

<sup>a</sup>As recognized by the HUGO Gene Nomenclature Committee ([www.gene.ucl.ac.uk/nomenclature/](http://www.gene.ucl.ac.uk/nomenclature/)); <sup>b</sup>*MIC2* product.

The purpose of this monograph is to describe the ISBT terminology for red cell surface antigens and to tabulate the complete current version of the classification. Much of the information provided in the 1995 monograph [1] is reiterated here so that referral back will not generally be required, but only references published after 1995 are provided.

### The ISBT numerical terminology

The mandate of the Committee is to provide a numerical terminology for red cell surface antigens. By definition, these antigens must be defined serologically by the use of a specific antibody. Numerical designations and blood group symbols cannot be allocated to nucleotide or amino acid sequences or polymorphisms, even though the presence of specific blood group antigens may be indicated by these techniques. All antigens receiving ISBT numbers must have been shown to be inherited characters.

All authenticated antigens fall into one of four classifications: systems; collections; low-incidence antigens (700 series); and high-incidence antigens (901 series). A blood group system consists of one or more antigens controlled at a single gene locus, or by two or more very closely linked homologous genes with little or no observable recombination between them. Each system has been shown to be genetically discrete from every other system. Collections consist of serologically, biochemically, or genetically related antigens, which do not fit the criteria required for system status. The 700 and 901 series contain low- and high-incidence antigens, respectively, which cannot be included in a system or collection.

Each antigen belonging to a blood group system is identified by a six-digit number (Tables 1–3). The first three digits represent the system (e.g. 006 for Kell) and the second three the specificity (e.g. 006003 for Kp<sup>a</sup>). Alternatively, the system symbol followed by the antigen number may be used (e.g. KEL003 or, more usually, KEL3 as sinistral zeros may be

**Table 2** Examples of antigen, phenotype, gene, and genotype designations in International Society of Blood Transfusion (ISBT) and traditional terminologies

|           | ISBT                                | Traditional and 'popular' alternative   |
|-----------|-------------------------------------|---|
| Antigen   | LU1 or 005001                       | Lu <sup>a</sup>   |
| Phenotype | LU:-1,2                             | Lu(a-b+)  |
| Gene      | <i>LU*1</i>                         | <i>Lu<sup>a</sup></i>   |
| Genotype  | <i>LU*2/2</i><br><i>LU*1,8/2,14</i> | <i>Lu<sup>b</sup>/Lu<sup>b</sup></i><br><i>Lu<sup>a</sup>Lu<sup>8</sup>/Lu<sup>b</sup>Lu<sup>14</sup></i> |

removed). Phenotypes are represented by the system symbol, followed by a colon, followed by a list of antigens separated by commas. Those antigens shown to be absent are preceded by a minus sign (e.g. *KEL*:-1,2,-3,4). Genes are designated by the system symbol, followed by an asterisk, followed by the antigen number (e.g. *KEL\*3*). Genotypes have the system symbol, followed by an asterisk, followed by alleles or haplotypes separated by a slash (e.g. *KEL\*2,3/2,4*). Amorph or null genes are represented by a zero (e.g. *KEL\*2,3/0*). Gene and genotype designations are italicized (or underlined). Antigen, phenotype, gene and genotype designations for collections are constructed in the same way. For the 700 and 901 series, 700 or 901 replaces the system symbol.

### Symbols for gene loci

The symbol for a gene or cluster of genes controlling a blood group system is the italicized symbol for the system (e.g. *CO* for the gene controlling the Colton system). The genes controlling all of the blood group systems have been cloned and, in many cases, the gene locus has an alternative symbol (Table 1), usually because the protein product of the gene is of known function or the gene had an existing symbol before the association with the blood group was known. Examples: the genes controlling expression of the Diego and Kidd antigens encode solute carriers with the symbols *SLC4A1* and *SLC14A1*, respectively; the Yt antigens are encoded by the acetylcholinesterase gene *ACHE*; the Colton and GIL antigens are encoded by *AQP1* and *AQP3*, respectively, the genes producing the water transporters Aquaporin-1 and -3; the presence of H antigen on the red cells is determined by an  $\alpha$ -1,2-fucosyltransferase gene, *FUT1*; and the presence of Lewis antigens on red cells is indirectly determined by an  $\alpha$ -1,3/4-fucosyltransferase gene, *FUT3*. At least two genes, *RHD* and *RHCE*, govern the Rh antigens, and three genes, *GYPB*, *GYPB*, and *GYPE*, are involved in the expression of antigens of the MNS system. The symbol for the gene governing a serologically determined blood group antigen comprises the system symbol and antigen number (e.g. *RH\*1*, *DI\*2*, *CO\*1*). When the gene encoding a blood group antigen is

determined by non-serological means, such as nucleotide sequencing, the alternative symbol should be used (e.g. *SLC14A1* instead of *JK*, and *DAF* instead of *CROM*) and allele designations should conform to the established terminologies employed for nucleotide polymorphisms (see refs 24,25 and [www.bioc.aecom.yu.edu/bgmnt/index.htm](http://www.bioc.aecom.yu.edu/bgmnt/index.htm)).

It is important to remember that when symbols such as *RH\*2* or *MNS\*10* are used, the symbol does not necessarily represent a single defined gene, but one of a cluster of genes or a hybrid of two genes.

### A 'popular', alternative terminology

The numerical terminology was devised primarily for computer storage of information on blood group antigens and to provide a framework for a genetical classification. The numerical terminology is not suitable for everyday communication and many scientists working in the field of human blood groups prefer not to use it in publications. This has led to a variety of alternative names being used for some blood group antigens. In an attempt to introduce some uniformity, a recommended list of alternative names for antigens is provided in Table 3. In most cases, the name or symbol is identical to that originally published, but in a few cases the more commonly used name is provided. In addition, there are recommended formats for describing phenotypes in the alternative terminology. These mostly employ traditional terminology, and examples are shown in Table 4. A more complete list has been published previously [4].

### Blood group systems

There are currently 29 systems containing a total of 245 antigens (Tables 1 and 3).

#### Modifications since 1995: existing systems

##### *002, the MNS system*

Five new antigens have been added. Absence of the high-incidence antigen MNS39 (ENEP) and presence of the low-incidence antigen MNS41 (HAG) is associated with an Ala65Pro substitution in glycophorin A (GPA) [26]. The absence of MNS42 (ENAV, previously AVIS) and the presence of MNS43 (MARS), its low-incidence antithetical antigen, results from a Gln63Lys substitution in GPA [27]. Both of these substitutions are associated with abnormal expression of DI4 (Wr<sup>b</sup>). MNS40 (ENEH) is absent from glycophorin A of the phenotype GP.Vw (Mi.I); the glycophorin A has a Thr28Met substitution and expresses MNS9 (Vw) antigen [28].

##### *003, the P system*

Evidence was presented suggesting that the same transferase encoded by *A4GALT*, is responsible for the biosynthesis of

**Table 3** Antigens of the blood group systems

| System | Antigen number |                 |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
|--------|----------------|-----------------|-----------------|------------------|------------------|--------------------|------------------|-----------------|------------------|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|-----------------|-----------------|-----|----------------|-----|
|        | 001            | 002             | 003             | 004              | 005              | 006                | 007              | 008             | 009              | 010              | 011             | 012             | 013             | 014             | 015             | 016             | 017             | 018             | 019             | 020              | 021             | 022             | 023 | 024            |     |
| 001    | ABO            | A               | B               | A,B              | A1               | ...                |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 002    | MNS            | M               | N               | S                | s                | U                  | He               | Mi <sup>a</sup> | M <sup>c</sup>   | Vw               | Mur             | M <sup>g</sup>  | Vr              | M <sup>e</sup>  | Mt <sup>a</sup> | St <sup>a</sup> | Ri <sup>a</sup> | Cl <sup>a</sup> | Ny <sup>a</sup> | Hut              | Hil             | M <sup>v</sup>  | Far | s <sup>D</sup> | Mit |
| 003    | P              | P1              | ...             | ...              |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 004    | RH             | D               | C               | E                | c                | e                  | f                | Ce              | C <sup>w</sup>   | C <sup>x</sup>   | V               | E <sup>w</sup>  | G               | ...             | ...             | ...             | ...             | Hr <sub>o</sub> | Hr              | hr <sup>S</sup>  | VS              | C <sup>G</sup>  | CE  | D <sup>w</sup> | ... |
| 005    | LU             | Lu <sup>a</sup> | Lu <sup>b</sup> | Lu3              | Lu4              | Lu5                | Lu6              | Lu7             | Lu8              | Lu9              | ...             | Lu11            | Lu12            | Lu13            | Lu14            | ...             | Lu16            | Lu17            | Au <sup>a</sup> | Au <sup>b</sup>  | Lu20            | Lu21            |     |                |     |
| 006    | KEL            | K               | k               | Kp <sup>a</sup>  | Kp <sup>b</sup>  | Ku                 | Js <sup>a</sup>  | Js <sup>b</sup> | ...              | ...              | UI <sup>a</sup> | K11             | K12             | K13             | K14             | ...             | K16             | K17             | K18             | K19              | Km              | Kp <sup>c</sup> | K22 | K23            | K24 |
| 007    | LE             | Le <sup>a</sup> | Le <sup>b</sup> | Le <sup>ab</sup> | Le <sup>bH</sup> | ALe <sup>b</sup>   | BLE <sup>b</sup> |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 008    | FY             | Fy <sup>a</sup> | Fy <sup>b</sup> | Fy3              | Fy4              | Fy5                | Fy6              |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 009    | JK             | Jk <sup>a</sup> | Jk <sup>b</sup> | Jk3              |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 010    | DI             | Di <sup>a</sup> | Di <sup>b</sup> | Wr <sup>a</sup>  | Wr <sup>b</sup>  | Wd <sup>a</sup>    | Rb <sup>a</sup>  | WARR            | ELO              | Wu               | Bp <sup>a</sup> | Mo <sup>a</sup> | Hg <sup>a</sup> | Vg <sup>a</sup> | Sw <sup>a</sup> | BOW             | NFLD            | Jn <sup>a</sup> | KREP            | Tr <sup>a*</sup> | Fr <sup>a</sup> | SW1             |     |                |     |
| 011    | YT             | Yt <sup>a</sup> | Yt <sup>b</sup> |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 012    | XG             | Xg <sup>a</sup> | CD99            |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 013    | SC             | Sc1             | Sc2             | Sc3              | Rd               | STAR               |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 014    | DO             | Do <sup>a</sup> | Do <sup>b</sup> | Gy <sup>a</sup>  | Hy               | Jo <sup>a</sup>    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 015    | CO             | Co <sup>a</sup> | Co <sup>b</sup> | Co3              |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 016    | LW             | ...             | ...             | ...              | ...              | LW <sup>a</sup>    | LW <sup>ab</sup> | LW <sup>b</sup> |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 017    | CH/RG          | Ch1             | Ch2             | Ch3              | Ch4              | Ch5                | Ch6              | WH              |                  |                  |                 | Rg1             | Rg2             |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 018    | H              | H               |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 019    | XK             | Kx              |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 020    | GE             | ...             | Ge2             | Ge3              | Ge4              | Wb                 | Ls <sup>a</sup>  | An <sup>a</sup> | Dh <sup>a</sup>  | GEIS             |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 021    | CROM           | Cr <sup>a</sup> | Tc <sup>b</sup> | Tc <sup>c</sup>  | Tc <sup>c</sup>  | Dr <sup>a</sup>    | Es <sup>a</sup>  | IFC             | WES <sup>a</sup> | WES <sup>b</sup> | UMC             | GUTI            | SERF            | ZENA            |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 022    | KN             | Kn <sup>a</sup> | Kn <sup>b</sup> | McC <sup>a</sup> | SI1              | Yk <sup>a</sup>    | McC <sup>b</sup> | SI2             | SI3*             |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 023    | IN             | In <sup>a</sup> | In <sup>b</sup> |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 024    | OK             | Ok <sup>a</sup> |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 025    | RAPH           | MER2            |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 026    | JMH            | JMH             |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 027    | I              | I               |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 028    | GLOB           | P               |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 029    | GIL            | GIL             |                 |                  |                  |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
|        |                | 025             | 026             | 027              | 028              | 029                | 030              | 031             | 032              | 033              | 034             | 035             | 036             | 037             | 038             | 039             | 040             | 041             | 042             | 043              | 044             | 045             | 046 |                |     |
| 002    | MNS            | Dantu           | Hop             | Nob              | En <sup>a</sup>  | En <sup>a</sup> KT | 'N'              | Or              | DANE             | TSEN             | MINY            | MUT             | SAT             | ERIK            | Os <sup>a</sup> | ENEP            | ENEH            | HAG             | ENAV            | MARS             |                 |                 |     |                |     |
| 004    | RH             | ...             | c-like          | cE               | hr <sup>H</sup>  | Rh29               | Go <sup>a</sup>  | hr <sup>B</sup> | Rh32             | Rh33             | hr <sup>B</sup> | Rh35            | Be <sup>a</sup> | Evans           | ...             | Rh39            | Tar             | Rh41            | Rh42            | Crawford         | Nou             | Riv             | Sec |                |     |
| 006    | KEL            | VLAN            | TOU             | RAZ              | VONG             |                    |                  |                 |                  |                  |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
|        |                | 047             | 048             | 049              | 050              | 051                | 052              | 053             | 054              | 055              | 056             |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |
| 004    | RH             | Dav             | JAL             | STEM             | FPTT             | MAR                | BARC             | JAHK            | DAK              | LOCR             | CENR            |                 |                 |                 |                 |                 |                 |                 |                 |                  |                 |                 |     |                |     |

... = obsolete (see Table 9); \*provisional.

**Table 4** Examples of the format recommended for phenotype designation in the alternative, 'popular' terminology

| Numerical terminology                 | Alternative terminology   |
|---------------------------------------|---|
| ABO:-1,-2,-3                          | O   |
| ABO:1,-2,3,4                          | A <sub>1</sub>  |
| ABO:1,-2,3,-4                         | A <sub>2</sub>  |
| MNS:1,2,-3,4,5,-6,7                   | M+ N+ S- s+ U+ He- Mi(a+) (in ISBT order)<br>Symbols such as Mi.III or GP.Mur, En(a-), M <sup>k</sup> are also acceptable   |
| P:1                                   | P1+ or P <sub>1</sub>   |
| P:-1                                  | P1- or P <sub>2</sub> (if shown to be GLOB:1)   |
| RH:1,2,-3,4,5,-8,32,33,-36            | D+ C+ E- c+ e+ C <sup>w</sup> - Rh:-32,33 Be(a-) (in ISBT order)<br>The order D C c E e would be an acceptable alternative. Probable genotypes as phenotypes (e.g. R <sub>1</sub> R <sub>2</sub> or DCE/DcE; R <sub>1</sub> r C <sup>w</sup> + or DCE/dce C <sup>w</sup> +) are acceptable, providing it is made clear that they are only probable genotypes based on haplotype frequencies.<br>Null and mod phenotypes: Rh <sub>null</sub> ; Rh <sub>mod</sub> |
| LU:-1,2,3,4                           | Lu(a-b+) Lu:3,4.<br>Null phenotype: Lu <sub>null</sub> or Lu(a-b-)  |
| KEL:-1,2,-3,4,5,-6,7,11,12,13,-17,-21 | K- k+ Kp(a-b+c-) Ku+ Js(a-b+) K:11,12,13,-17,-21<br>Null and mod phenotypes: K <sub>0</sub> or Kell <sub>null</sub> ; K <sub>mod</sub>  |
| FY:1,2,3                              | Fy(a+b+) Fy:3   |
| FY:-1,-2,-3                           | Fy(a-b-) Fy:-3<br>Fy <sup>x</sup> may be used as a phenotype  |
| DI:1,2,-3,4,-5,-6,-7                  | Di(a+b+) Wr(a-b+) Wd(a-) Rb(a-) WARR-   |
| DO:1,2,3,4,5                          | Do(a+b+) Gy(a+) Hy+ Jo(a+)  |
| LW:5,6,-7                             | LW(a+b-) LW(ab+)  |
| CH/RG:1,2,-7,11,12                    | Ch:1,2 WH- Rg:1,2   |
| H:-1                                  | H - The symbol O <sub>n</sub> may be used for the true Bombay phenotype (red cells totally H-deficient, ABH non-secretors). Otherwise the terms 'Red cell H-deficient secretor' and 'Red cell H-deficient non-secretor' are recommended.  |
| XK:-1                                 | Kx- or McLeod   |
| GE:2,3,4,-5,-6,-7,-8,-9               | Ge:2,3,4 Wb- Ls(a-) An(a-) Dh(a-) GEIS-   |
| GE:-2,-3,4                            | Ge:-2,-3,4 or Gerbich phenotype   |
| GE:-2,3,4                             | Ge:-2,3,4 or Yus phenotype  |
| GE:-2,-3,-4                           | Ge:-2,-3,-4 or Leach phenotype  |
| RAPH:1                                | MER2+   |
| I:1                                   | I adult   |
| I:-1                                  | i adult or cord   |

both P1 and P<sup>k</sup> (209002 of the GLOB Collection) [29]. However, because of reports of conflicting evidence [30] (L. Tilley, G. Daniels, unpublished) P<sup>k</sup> has not joined the P system.

#### 004, the Rh system

Five antigens of low incidence have been added: RH52 (BARC) is produced by most D<sup>Vl</sup>Ce haplotypes, but is not produced by D<sup>Vl</sup>cE haplotypes [31]; RH53 (JAHK) is associated with the rare Rh phenotype r<sup>G</sup> [32]; RH54 (DAK) with DIIIa, DOL, and some other rare Rh phenotypes [33]; RH55 (LOCR, previously 700053) with weak expression of RH4 (c) and RH5 (e) [34]; and RH56 (CENR) with an RHCE-D hybrid gene associated with RH8 (C<sup>w</sup>) and altered expression of RH2 (C) and RH5 (e) [35].

A new terminology has been devised for epitopes of RH1 (D) [36]. Basically, each epitope has two numbers, one representing the conventional epD1 to epD9 system proposed by

Lomas *et al.* [37], the other representing subdivisions of those numbers. The complete numerical terminology for epD1 is 004001.001.001 (abbreviated to epD1.1) and the epD1 subsplit caused by DFR is 004001.001.002 (epD1.2). Partial D antigens will be designated by up to four upper case letters or Roman numerals on the line; for example DIIIa, DIV, DHAR, DFR.

#### 005, the Lutheran system

Absence of a new Lutheran antigen of high incidence, LU21, is associated with homozygosity for an LU mutation encoding Asp94Glu [38].

#### 006, the Kell system

KEL25 (VLAN) and KEL28 (VONG) are low-incidence antigens associated with Arg248Gln and Arg248Trp, respectively, in the Kell glycoprotein [39,40]. KEL26 (TOU) and KEL27 (RAZ)

are antigens of high incidence, absent from the Kell glycoprotein with Arg406Gln [41] and Glu299Lys [39] substitutions, respectively.

#### 007, the Lewis system

Three antigens, previously known for many years, were added to this system. LE4 (Le<sup>bH</sup>) is defined by antibodies that react with LE:2 [Le(b+)] cells, but only when H1 (H) is strongly expressed (group O and A<sub>2</sub> phenotypes). LE5 (ALe<sup>b</sup>) and LE6 (BLE<sup>b</sup>) are expressed when A type 1 and B type 1 are modified by the product of the Lewis gene, *FUT3* [42].

#### 010, the Diego system

Seventeen new antigens have been added, all of low incidence and all associated with mutations in *SLC4A1* encoding amino acid substitutions in the erythrocyte anion exchanger (Table 5). The DI19 designation for Tr<sup>a</sup> is still provisional because only one case was analysed.

#### 012, the Xg system

CD99, a glycoprotein encoded by a gene on both X and Y chromosomes, is recognized by monoclonal antibodies and human alloantibodies [54,55]. *MIC2*, the structural gene for CD99, is closely linked to *XG* and shares substantial sequence homology with *XG*. Consequently, CD99 became *XG2*.

#### 013, the Scianna system

Following the discovery that the Scianna antigens are expressed by the red cell adhesion protein, human ERMAP, expression of the low-incidence antigen, 700015 (Rd), was found to be associated with a mutation in *ERMAP* encoding

Pro60Ala [9]. 700015 has become SC4. A new antigen of high incidence, STAR, is associated with Glu47Lys in ERMAP [56] and numbered SC5.

#### 018, the Hh system

The system name has been changed to H.

#### 020, the Gerbich system

A new antigen of low incidence, GEIS, associated with Thr32Asn in GPC and Thr11Asn in GPD [57], has been numbered GE9.

#### 021, the Cromer system

Three new antigens of high incidence have been added: CROM11 (GUTI) [58], CROM12 (SERF) [59], and CROM13 (ZENA) [60] are associated with Arg206His, Pro182Leu and His208Gln in CD55, respectively.

#### 022, the Knops system

Three new antigens have been added: KN6 to KN8. KN6 (McC<sup>b</sup>) represents Lys1590Glu in CD35, which is also associated with the absence of KN3 (McC<sup>a</sup>) [61]. KN4 (previously SI<sup>a</sup>, now SI1) requires Arg1601 on CD35, KN7 (previously Vil, now SI2) requires Gly1601, and KN8 (SI3) requires both Arg1601 and Ser1610 [61,62]. The number KN8 is provisional because further complications are predicted.

### Modifications since 1995: new systems

#### 024, the Ok system

The high-incidence antigen OK1 (Ok<sup>a</sup>, previously 901006) became the sole antigen of the Ok system following identification of the gene (*BSG*) encoding the protein and of the amino acid substitution (Glu92Lys) responsible for the OK:-1 phenotype [12].

#### 025, the Raph system

This new system contains one antigen: RAPH1 (MER2, previously 901011). Distinction of RAPH from the other blood group systems was demonstrated by family studies and by the positioning of *CD151*, the controlling gene, at 11p15.5 [13–15].

#### 026, the John Milton Hagen system

JMH1 (JMH, previously 901007) is carried on the semaphorin CD108 [16]. The gene encoding CD108, *SEMA7A*, is located on the long arm of chromosome 15 [17], which distinguishes JMH1 from all existing blood group systems. JMH1 represents the antigen detected by antibodies produced by JMH:-1 individuals.

#### 027, the I system

*GCNT2*, the gene encoding the *N*-acetylglucosaminyltransferase responsible for converting i-active straight chains to

**Table 5** Antigens of the Diego System assigned since 1995

| Antigen |                  | Previous number | Amino acid substitution | References |
|---------|------------------|-----------------|-------------------------|------------|
| DI5     | Wd <sup>a</sup>  | 700030          | Val557Met               | [43,44]    |
| DI6     | Rb <sup>a</sup>  | 700027          | Pro548Leu               | [44]       |
| DI7     | WARR             | 700055          | Thr552Ile               | [45]       |
| DI8     | ELO              | 700051          | Arg432Trp               | [46,47]    |
| DI9     | Wu               | 700013          | Gly565Ala               | [48]       |
| DI10    | Bp <sup>a</sup>  | 700010          | Asn569Lys               | [47]       |
| DI11    | Mo <sup>a</sup>  | 700022          | Arg656His               | [47]       |
| DI12    | Hg <sup>a</sup>  | 700034          | Arg656Cys               | [47]       |
| DI13    | Vg <sup>a</sup>  | 700029          | Tyr555His               | [47]       |
| DI14    | Sw <sup>a</sup>  | 700004          | Arg646Gln or Trp        | [49]       |
| DI15    | BOW              | 700046          | Pro561Ser               | [47,50,51] |
| DI16    | NFLD             | 700037          | Glu429Asp, Pro561Ala    | [51]       |
| DI17    | Jn <sup>a</sup>  | 700014          | Pro566Ser               | [52]       |
| DI18    | KREP             |                 | Pro566Ala               | [50]       |
| DI19    | Tr <sup>a*</sup> | 700008          | Lys551Asn               | [44]       |
| DI20    | Fr <sup>a</sup>  | 700026          | Glu480Lys               | [53]       |
| DI21    | SW1              | 700041          | Arg646Trp               | [49]       |



I-active branched chains, has been cloned and some mutations responsible for the *i* adult phenotype identified [18,19]. I1 antigen (I, previously 207001) is the only antigen of the I system. The *i* antigen, the precursor of I1, provisionally remains as 207002.

#### 028, the Globoside system

The gene (*B3GALT3*) encoding the *N*-acetylgalactosaminyl-transferase (globoside synthase) responsible for converting P<sup>k</sup> (209002) to P (previously 209001, globoside) has been cloned and inactivating mutations responsible for the P<sup>k</sup> (P-negative) phenotype have been identified [20,21]. P has become GLOB1, the only antigen of the Globoside system.

#### 029, the GIL system

GIL1, the only antigen of the GIL system, is an antigen of high incidence located on the glycerol transporter aquaporin 3, and the GIL:-1 phenotype results from an inactivating mutation within the *AQP3* gene [22,23]. *AQP3* is on chromosome 9p13, so GIL is genetically discrete from all other blood group systems.

### Guidelines for the establishment of new blood group systems

For an antigen to form a new blood group system it must be defined by a human alloantibody, be an inherited character, the gene encoding it must have been identified and sequenced, and its chromosomal location must be known. In addition, the gene must be different from, and not a closely linked homologue of, all other genes encoding antigens of existing blood group systems.

All established blood group systems meet these criteria.

### Guidelines for the inclusion of a new specificity in an established system

All antigens awarded an ISBT number must have been shown to be inherited, and at least one of the following four criteria must be met.

(1) An antithetical relationship between a new antigen and one already assigned to the system.

(2) Demonstration that expression of the antigen is associated with a variation in the nucleotide sequence of the gene controlling the system.

(3) Evidence, from a linkage analysis of family data, that the controlling allele is probably a newly recognized form of the pertinent gene, and supporting serological or biochemical information.

(4) Demonstration that an antigen is located on a protein or glycoprotein that carries other antigens belonging to the system. It must be remembered, however, that this could result from post-translational modification of a gene

product, such as glycosylation, which would not support inclusion within the system.

### Blood group collections

There are six blood group collections (Table 6).

A new Collection, 211 or Vel, was created to include two serologically related antigens of high incidence, Vel (VEL1, previously 901001) and ABTI (VEL2, previously 901015) [63,64].

An antibody produced by a patient with ER:-1,-2 red cells and with the characteristics of antibodies of the ER Collection reacted with ER:1,-2, ER:-1,2, and the only other example of ER:-1,-2 red cells [65]. The antigen recognized by this antibody has become ER3 (208003) of the ER Collection.

Since 1995, 207001 (I1, I) has formed the I system and retains the symbol I1, and 209001 (GLOB1, P) has formed the Globoside system and retains the symbol GLOB1. The creation of the I and Globoside systems means that these two systems have identical symbols, I and GLOB, to those of Collections 207 and 209. This should not cause confusion, however, as I1 and GLOB1 cannot refer to 207001 and 209001, as those numbers are now obsolete. Collection 207 now contains only one antigen. These anomalies will be resolved when a separate carbohydrate collection is created.

### 700 series, low-incidence antigens

There are currently 19 antigens in the 700 series (Table 7). Since 1995, no new numbers have been added and 18 numbers have been made obsolete: 16 antigens have joined the Diego

**Table 6** Collections of antigens

| Collection |      |        | Antigen |                 |                      |
|------------|------|--------|---------|-----------------|----------------------|
| No.        | Name | Symbol | No.     | Symbol          | Incidence percentage |
| 205        | Cost | COST   | 205001  | Cs <sup>a</sup> | 95                   |
|            |      |        | 205002  | Cs <sup>b</sup> | 34                   |
| 207        | li   | I      | 207002  | <i>i</i>        | *                    |
| 208        | Er   | ER     | 208001  | Er <sup>a</sup> | > 99                 |
|            |      |        | 208002  | Er <sup>b</sup> | < 1                  |
|            |      |        | 208002  | Er3             | > 99                 |
| 209        |      | GLOB   | 209002  | P <sup>k</sup>  | > 99*                |
|            |      |        | 209003  | LKE             | 98                   |
| 210        |      |        | 210001  | Le <sup>c</sup> | 1                    |
|            |      |        | 210002  | Le <sup>d</sup> | 6                    |
| 211        | Vel  | VEL    | 211001  | Vel             | > 99                 |
|            |      |        | 211002  | ABTI            | > 99                 |

\*By standard serological tests, may appear to be low incidence. Obsolete collections: 201 Gerbich; 202 Cromer; 203 Indian; 204 Auberger; 206 Gregory; 211 Wright.

**Table 7** The700 series: low-incidence antigens

| No.    | Name         | Symbol           | No.    | Name      | Symbol          |
|--------|--------------|------------------|--------|-----------|-----------------|
| 700002 | Batty        | By               | 700040 | Rasmussen | RASM            |
| 700003 | Christiansen | Chr <sup>a</sup> | 700043 | Oldeide   | Oj <sup>a</sup> |
| 700005 | Biles        | Bi               | 700044 |           | JFV             |
| 700006 | Box          | Bx <sup>a</sup>  | 700045 | Katagiri  | kg              |
| 700017 | Torkildsen   | To <sup>a</sup>  | 700047 | Jones     | JONES           |
| 700018 | Peters       | Pt <sup>a</sup>  | 700049 |           | HJK             |
| 700019 | Reid         | Re <sup>a</sup>  | 700050 |           | HOFM            |
| 700021 | Jensen       | Je <sup>a</sup>  | 700052 |           | SARA            |
| 700028 | Livesay      | Li <sup>a</sup>  | 700054 |           | REIT            |
| 700039 | Milne        |                  |        |           |                 |

**Table 8** The 901 series: high-incidence antigens

| No.    | Name      | Symbol          | No.    | Name   | Symbol          |
|--------|-----------|-----------------|--------|--------|-----------------|
| 901002 | Langereis | Lan             | 901012 | Sid    | Sd <sup>a</sup> |
| 901003 | August    | At <sup>a</sup> | 901013 | Duclos |                 |
| 901005 |           | Jr <sup>a</sup> | 901014 |        | PEL             |
| 901008 |           | Emm             | 901016 |        | MAM             |
| 901009 | Anton     | AnWj            |        |        |                 |

system (Table 5); 700015 (Rd) has become SC4; and 700053 (LOCR) has become RH55.

### Criteria for inclusion in the 700 series:

- (1) An incidence of < 1% in most populations tested.
- (2) Distinction from all other numbered low-incidence antigens of the 700 series as well as those of the blood group systems and collections.
- (3) Demonstration of inheritance through at least two generations.

### 901 series, high-incidence antigens

There are currently nine antigens in the 901 series (Table 8). Since 1995, two new antigens, both of high incidence, have been added: 901015 (ABTI) [63] and 901016 (MAM) [66], although 901015 (ABTI) has now become VEL2 of the 211 collection. Three antigens became the sole antigens of new blood group systems and their 901 numbers are obsolete: 901006 (Ok<sup>a</sup>) has become OK1; 901007 (JMH) has become JMH1; and 901011 (MER2) has become RAPH1 (Table 1).

The gene encoding the  $\beta$ 1,4-*N*-acetylgalactosaminyltransferase responsible for 901012 (Sd<sup>a</sup>) antigen has been cloned [67,68], but 901012 has not formed a new blood group system because the molecular basis for the Sd<sup>a</sup> polymorphism has not been determined.

### Criteria for inclusion in the 901 series:

- (1) An incidence of > 90% in most populations tested.
- (2) Distinction from all other numbered high-incidence specificities.
- (3) Demonstration that the antigen is lacking from the red cells of at least 2 sibs, i.e. that the negative phenotype is genetically determined.

### Obsolete numbers

There is no recycling of blood group numbers: once a number has been allocated to a specificity, that number cannot be subsequently used for any other specificity. Consequently, if the number of a specificity becomes inappropriate, then that number becomes obsolete. Obsolete numbers are listed in Table 9.

### Procurement of ISBT numerical designations

#### Choice of symbol

Symbols for designations of new specificities will consist of three to six on-line capital letters and must not duplicate, alphabetically or phonetically, any current or obsolete symbols shown in the tables. Also, symbols used in related fields, such as those used for platelet and leucocyte antigens, must be avoided. Symbols for specificities that may herald new blood group systems, and thus new genes, have the further constraint that they must differ from any symbols given to genes by the HUGO Nomenclature Committee (<http://www.gene.ucl.ac.uk/nomenclature/>).

#### Procedures for acquisition of an ISBT number

The initial stipulation is that materials for defining the new specificity should be available for either circulation or in-house testing; the futility of defining a new specificity from which future new specificities cannot be distinguished is obvious. Proposals should be submitted with supporting data to the members of the Committee listed below, who are authorized to allocate numbers provisionally in consultation with the Chair. All decisions must be ratified by the Committee before being finalized.

- For a new blood group system or collection: Dr Geoff Daniels.
- For a specificity number within an established system: Dr Marion Reid for the MNS system; Dr Sylvano Wendel or Mrs Marilyn Moulds for the Rh system; Dr Jan Jørgensen for other systems.
- For a specificity number in a current collection: Dr Geoff Daniels.
- For a 700 number: Dr Teresa Zelinski.
- For a 901 number: Dr Geoff Daniels.



**Table 9** Obsolete numbers

| Obsolete no.   | Symbol or previous symbol   | Current no.             | Obsolete no. | Symbol or previous symbol            | Current no. |
|----------------|-----------------------------|-------------------------|--------------|--------------------------------------|-------------|
| 001005         | H                           | 018001                  | 700010       | Bp <sup>a</sup>                      | 010010      |
| 003002         | P                           | 209001                  | 700011       | Or                                   | 002031      |
| 003003         | P <sup>k</sup>              | 209002                  | 700012       | Gf                                   | Obsolete    |
| 004013         | Rh <sup>A</sup>             | Obsolete                | 700013       | Wu                                   | 010009      |
| 004014         | Rh <sup>B</sup>             | Obsolete                | 700014       | Jn <sup>a</sup>                      | 010017      |
| 004015         | Rh <sup>C</sup>             | Obsolete                | 700015       | Rd                                   | 013004      |
| 004016         | Rh <sup>D</sup>             | Obsolete                | 700016       | Heibel                               | Obsolete    |
| 004024         | E <sup>T</sup>              | Obsolete                | 700020       | An <sup>a</sup>                      | 020007      |
| 004025         | LW                          | Obsolete, see system 16 | 700022       | Mo <sup>a</sup>                      | 010011      |
| 004038         | Duclos                      | 901013                  | 700023       | Hey                                  | Obsolete    |
| 005010         | Singleton                   | Obsolete                | 700024       | Ri <sup>a</sup> (= Ls <sup>a</sup> ) | 020006      |
| 005015         | Anton                       | 901009                  | 700025       | In <sup>a</sup>                      | 023001      |
| 006008         | Kw                          | Obsolete                | 700026       | Fr <sup>a</sup>                      | 010020      |
| 006009         | KL                          | Obsolete                | 700027       | Rb <sup>a</sup>                      | 010006      |
| 006015         | Kx                          | 019001                  | 700029       | Vg <sup>a</sup>                      | 010013      |
| 016001         | LW <sub>1</sub> phenotype   | Obsolete                | 700030       | Wd <sup>a</sup>                      | 010005      |
| 016002         | LW <sub>2</sub> phenotype   | Obsolete                | 700031       | Dh <sup>a</sup>                      | 020008      |
| 016003         | LW <sub>3</sub> phenotype   | Obsolete                | 700032       | POLL                                 | Obsolete    |
| 016004         | LW <sub>4</sub> phenotype   | Obsolete                | 700033       | Os <sup>a</sup>                      | 002038      |
| 020001         | Ge1                         | Obsolete                | 700034       | Hg <sup>a</sup>                      | 010012      |
| Collection 201 | GE                          | System 020              | 700035       | Tc <sup>b</sup>                      | 021003      |
| Collection 202 | CROMER                      | System 021              | 700036       | Tc <sup>c</sup>                      | 021004      |
| Collection 203 | IN                          | System 023              | 700037       | NFLD                                 | 010016      |
| Collection 204 | AU                          | 005018 & 005019         | 700038       | Hov (= Wu)                           | 700013      |
| 205003         | Yk <sup>a</sup>             | 022005                  | 700041       | SW1                                  | 010021      |
| 205004         | Kn <sup>a</sup>             | 022001                  | 700042       | WES (WES <sup>a</sup> )              | 021008      |
| 205005         | Kn <sup>b</sup>             | 022002                  | 700046       | BOW                                  | 010015      |
| 205006         | McC <sup>a</sup>            | 022003                  | 700048       | FPTT                                 | 004050      |
| 205007         | Si <sup>a</sup>             | 022004                  | 700051       | ELO                                  | 010008      |
| Collection 206 | GY                          | 014003 & 014004         | 700053       | LOCR                                 | 004055      |
| 207001         | I                           | 027001                  | 700055       | WARR                                 | 010007      |
| Collection 211 | WR                          | 010003 & 010004         | 901004       | Jo <sup>a</sup>                      | 014005      |
| 209001         | P                           | 028001                  | 901006       | Ok <sup>a</sup>                      | 024001      |
| 700001         | W <sub>r</sub> <sup>a</sup> | 010003                  | 901007       | JMH                                  | 026001      |
| 700004         | Sw <sup>a</sup>             | 010013                  | 901010       | W <sub>r</sub> <sup>b</sup>          | 010004      |
| 700007         | Ls <sup>a</sup>             | 020006                  | 901011       | MER2                                 | 025001      |
| 700008         | Tr <sup>a</sup>             | 010019                  | 901001       | Vel                                  | 211001      |
| 700009         | Wb                          | 020005                  | 901015       | ABTI                                 | 211002      |

## Conclusions

Although the primary function of the Committee is to monitor and update the terminology, there are two main issues that need to be tackled in the future: updating and redefining the terminology for blood group genes and alleles; and devising a collection for those carbohydrate antigens that do not belong to a system.

The Committee strongly urges that all authors in the field of human red cell blood groups should use the terminology provided in Tables 1–8 in either the alphabetical/numerical

format (e.g. FY2) or the 'popular' alternative format (e.g. Fy<sup>b</sup>). For clarity, it is often advisable when using the more traditional terminology to include the ISBT terminology in parentheses, for example An<sup>a</sup> (GE7).

All members of the Committee, listed in Appendix I, are prepared to handle requests for advice or assistance in any aspect of an investigation or to direct them to the most appropriate authority. The Chair of the Committee would be happy to receive any comments or criticisms of the terminology and would raise them at a Committee meeting. Membership of the Committee is open to colleagues who are considered

international experts in the field of blood groups or related fields and who are prepared to participate in the activities of the Committee.

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## Appendix I

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