PROPOSALS ON NOMENCLATURE OF PROTEIN POLYMORPHISMS IN FARM LIVESTOCK

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Received December 12, 1966

AT the first meeting of the F.A.O. Panel of Blood Group Scientists held in The Hague, Netherlands, on 9th-11th September 1963, a Committee on Protein Polymorphism Nomenclature was appointed to consider protein polymorphism nomenclature in farm animals (F.A.O., 1963). The proposals of the Committee were circulated among workers in the field, and appeared in "Immunogenetics Letter" (ASHTON, GILMOUR, KIDDY and KRISTJANSSON 1966). The final version printed here includes many of the suggestions received from individuals who read the circulated proposals, and we are grateful for their comments. In preparing these recommendations, we were influenced by published rules or suggestions for nomenclature in related disciplines (BRAEND 1965; COHEN and SHREFFLER 1961; COMMITTEE ON STANDARDIZED GENETIC NOMENCLATURE FOR MICE, 1963; GERALD and INGRAM 1961; THOMPSON, *et al.*, 1965).

We recognize the right of individuals to report their results in such manner as they think best, with due deference to the priorities enjoyed by others. The recommendations below are meant to act as guidelines for research workers in the defined field who discover new protein polymorphisms, or new phenotypes in existing systems.

The need for standardization of nomenclature of these systems is closely associated with the need for provision of a source of reference samples. The committee appointed was asked to consider the feasibility of establishing a reference sample bank, initially for cattle. Preliminary plans for a bank in Wageningen, The Netherlands, and in Beltsville, Maryland, U.S.A., are now being implemented.

SCOPE OF THE COMMITTEE'S RECOMMENDATIONS

Polymorphism has been demonstrated in many proteins, both enzymes and nonenzymes, from a wide variety of biological fluids and tissues (blood plasma, blood cells, milk, saliva, sweat, urine, cerebrospinal fluid, seminal fluid, egg white, muscle, liver, kidney, skin, etc.). Our proposals are intended to apply generally to proteins, including enzymes, which can be demonstrated to occur in at least two phenotypic forms under genetic control. We have, however, specifically excluded immunoglobulins because guidelines for their nomenclature have

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been given for human immunoglobulins by CEPPELLINI *et al.* (W.H.O. 1965). For hemoglobins we think the proposals presented herein should apply until further information on their structure becomes available. At that time the recommendations of GERALD and INGRAM (1961) should be considered. We have also restricted our scope to a limited range of species commonly found as farm livestock, namely cattle, sheep, goats, horses, chickens, swine and turkeys. Our recommendations may also be helpful to individuals working with, for example, water buffalo, reindeer, rabbits, mink, quail and other domesticated mammals and birds.

Suggested rules for Genetic Nomenclature of Protein Polymorphisms within the Scope of the Committee's Recommendations

The rules for genetic nomenclature proposed are modelled on those of the COMMITTEE ON STANDARDIZED GENETIC NOMENCLATURE FOR MICE (1963), which in turn conform with standard usage in other species, including *Drosophila*.

We recommend that:

1. The names of genetic systems should be written with a lower case initial letter, except at the beginning of a sentence or other place in which capitals would normally be used. Examples: transferrin, haptoglobin, albumin. Whenever possible names should be based on a chemical identification or property.
2. The locus symbol applicable to both phenotype and genotype should commence with the initial letter of the gene name and should typically be an abbreviation of the gene name. The locus symbol should consist of the minimum number of letters necessary to ensure distinction from similar symbols. The locus symbol should be written in lower case letters with a capital initial letter, except when referring to a recessive or a "silent" allele when a lower case initial letter should be used.
3. Phenotypes which represent individual genotypes should be written in the form PpAB (nonitalicised) and the corresponding genotype in the form Pp^A/Pp^B or Pp^APp^B (italicised, diagonal optional) where here *Pp* represents the locus symbol. Examples: HbA and Hb^A/Hb^A or Hb^AHb^A , Alb FS and Alb^F/Alb^S or Alb^FAlb^S . Where the phenotype represents more than one genotype, it should be described by the locus symbol followed by a descriptive term: Examples: Pp fast; Pp +.
4. Symbols for alleles should be preferably capital letters, or alternatively Arabic numerals. Lower case letters are acceptable but less preferable. Examples: Tf^A , Hp^2 . An exception to this rule occurs in the naming of "new" alleles (see below).

We believe that this system of nomenclature will be applicable until the difference between alleles can be expressed in terms of molecular difference. At this time a more specific nomenclature will be needed, for which we suggest modifications appropriate to each case of the recommendations of GERALD and INGRAM (1961) for hemoglobin nomenclature.

NOMENCLATURE OF NEW PHENOTYPES

Two distinct situations arise in the detection of new phenotypes, dependent on whether the new type is clearly distinguishable from previously known types or whether the new type is detected as a result of an improvement in technique revealing heterogeneity of previously named types. The guidelines we suggest for naming the new phenotypes differ accordingly:

(a) *Clearly distinguishable new phenotypes.* If a previously undescribed phenotype is found in an existing system it should be compared with available reference samples, checked for phenotyping repeatability and stability, and checked for genetic relationship to other members of the system. If in the opinion of the investigator it constitutes a new phenotype in the particular system it should be named in a manner consistent with the established nomenclature for that system (see Table 1). To avoid confusion the investigator assigning a new letter or number should add a descriptive subscript, such as a location name. Example: a newly discovered cattle transferrin phenotype with zones corresponding to those produced by Tf^A together with zones from a presumed new allele discovered by a laboratory in Lima might be named Tf AJ_{Lima}. Providing no other laboratory used the letter J for a different new allele at the same time the Lima transferrin allele would eventually become known as cattle Tf^J .

This recommendation is made after due consideration of the conflicting demands of unambiguous but manageable terminology. Its usefulness depends on the promptness with which new alleles and phenotypes are reported by investigators.

In the event that the same letter or number is used by two laboratories for different alleles the authors concerned may wish to continue using the descriptive subscripts, or else they may agree to a mutually satisfactory compromise in terminology, preferably announced in a joint publication.

(b) *Heterogeneity in established phenotypes.* New phenotypes may be recognized as a result of improvements in technique which reveal variation in phenotypes previously considered homogeneous. An example is the splitting of zones sometimes encountered in apparently homozygous phenotypes, revealing them as heterozygotes.

Under these circumstances the gene symbol previously applied to the "homozygote" becomes ambiguous. Rather than use this symbol arbitrarily for one of the products of splitting we recommend that the original symbol should be applied to all the products of splitting, suitably modified. This assures continuity of nomenclature in the literature, but is not meant to imply any closer similarity between the products splitting than between the products of any other two alleles. If the system is one in which the various alleles are named alphabetically the Committee recommends that the modification should be by Arabic numerals, for example: Pp^B might give rise to Pp^{B1} and Pp^{B2} . Alternatively if the alleles are coded numerically, the modification could be by the addition of letters; e.g., Pp^{2A} and Pp^{2B} . Phenotypes should be written in the form PpB1B2, genotypes in the

form Pp^{B_1}/Pp^{B_2} or $Pp^{B_1}Pp^{B_2}$ (never in the form Pp^{B_1/B_2}), and alleles in the form Pp^{B_1} and Pp^{B_2} .

It is hoped that our recommendations for reference samples (involving only one ultimate reference animal for each allele) will diminish the need to invoke splitting nomenclature, at least in codominant systems.

NOMENCLATURE OF SYSTEMS AND LOCUS SYMBOLS

The naming of a new system, allocation of a locus symbol and naming of phenotypes is the prerogative of the discoverer(s), but we believe that the priority of these names and symbols should be governed by the Code of Ethics (Appendix A) of the International Code of Zoological Nomenclature (INTERNATIONAL COMMISSION ON ZOOLOGICAL NOMENCLATURE, 1961).

With increasing knowledge, a generalized name suitable for initial description may become outmoded. Examples: β -globulins (first used) and transferrins (now used) (GIBLETT, HICKMAN and SMITHIES 1959), thread-proteins (first used) and amylases (now used) (KING 1963). We recommend that a change in locus symbol should be announced in a scientific journal, signed by the authors holding priority for the original symbol and the discoverers of the information causing the change in symbol.

A new system may be discovered independently in more than one laboratory and assigned different nomenclatures. If this happens, the authors concerned are urged to seek mutual agreement about terminology and to publish details of the agreement as soon as possible.

LIST OF LOCUS AND GENE SYMBOLS

Table 1 shows a list of locus and gene symbols known to this Committee and used in the species of farm livestock considered. To the best of our knowledge the references listed include those of the authors holding priority for the symbol, but other relevant references are given in some instances. Among these are cases where two sets of nomenclature are in use because a uniform nomenclature has not been agreed. Correspondence between the sets is likely, but has not necessarily been confirmed. We wish to emphasize, however, that Table 1 is intended as an informative and not as an authoritative listing.

For many systems inter-laboratory comparisons have resulted in the establishment of a list of gene symbols each of which characterizes a different gene product. In the case of the cattle hemoglobins, extensive comparison between samples from different laboratories has not yet been performed. It is possible that different symbols have sometimes been allocated to the same gene product in this system.

REFERENCE SAMPLES

We realize that uniformity of nomenclature will be attained most rapidly by ready availability of reference samples. Unfortunately, it is only in codominant systems that unambiguity can be assured, and then only when any one allele is

TABLE 1

Published locus and gene symbols in current use for protein polymorphisms in certain species of livestock

Species	System name	Locus symbol	Gene symbols	Literature reference
<i>Bos taurus</i> and <i>Bos indicus</i>	haemoglobin	<i>Hb</i>	<i>A, B</i>	BANGHAM (1957)
			<i>C</i>	CROCKETT <i>et al.</i> (1963)
			<i>C_{Rhodesia}</i>	CARR (1964)
			<i>X</i>	NAIK <i>et al.</i> (1965)
			<i>D</i>	EFREMOV and BRAEND (1965)
	transferrin	<i>Tf</i>	<i>A, E</i>	ASHTON (1958a), SMITHIES and HICKMAN (1958)
			<i>B, F</i>	ASHTON (1959)
			<i>D1, D2</i>	KRISTJANSSON and HICKMAN (1965); ASHTON (1965a); JAMIESON (1965)
			<i>N</i>	GAHNE (1961)
			<i>G_{Kenya}</i>	ASHTON and LAMPKIN (1965)
			<i>G_{S.Africa}</i>	OSTERHOFF (1964)
			<i>H</i>	SARTORE and BERNOCO (1966)
			<i>F, S</i> }	BRAEND and EFREMOV (1965)
			<i>A, B</i> }*	ASHTON (1964)
			<i>C</i>	ASHTON and LAMPKIN (1965)
	post-albumin	<i>Pa</i>	<i>F, S</i>	ASHTON (1963); GAHNE (1963a)
	$S\alpha_2$ globulin	<i>S\alpha</i>	<i>A, O</i>	ASHTON (1958b)
	alkaline phosphatase	<i>F</i>	<i>A, O</i>	GAHNE (1963b)
	amylase	<i>Am</i>	<i>A, B, C</i>	ASHTON (1965b)
	carbonic anhydrase	<i>Ca</i>	<i>F, S</i>	SARTORE <i>et al.</i> (1967)
	β -lactoglobulin	<i>Lg</i>	<i>A, B</i>	ASCHAFFENBURG and DREWRY (1957)
			<i>C</i>	BELL (1962)
			<i>D</i>	MEYER (1966); GROSCLAUDE <i>et al.</i> (1966)
	α -lactalbumin	<i>La</i>	<i>A, B</i>	BLUMBERG and TOMBS (1958)
	β -casein	β - <i>Cn</i>	<i>B, C</i>	ASCHAFFENBURG (1963)
			<i>A1, A2, A3</i>	PETERSON and KOPFLER (1966); KIDDY <i>et al.</i> (1966)
	Ca-sensitive α -casein	α_{S1} - <i>Cn</i>	<i>A, B, C</i>	THOMPSON <i>et al.</i> (1962); KIDDY <i>et al.</i> (1964)
			<i>D</i>	GROSCLAUDE <i>et al.</i> (1966)
	κ -casein	κ - <i>Cn</i>	<i>A, B</i>	NEELIN (1964); WOYCHICK (1964); SCHMIDT (1964)
<i>Ovis domesticus</i>	haemoglobin	<i>Hb</i>	<i>A, B</i>	EVANS <i>et al.</i> (1956)
	transferrin	<i>Tf</i>	<i>A, B, C, D, E</i>	ASHTON (1958c)
			<i>G, N</i>	ASHTON and FERGUSON (1963)
			<i>P</i>	KHATTAB <i>et al.</i> (1964); NASRAT and OSTERLEE (1965)
			<i>I</i>	FESUS (1967)
			<i>M</i>	E.S.A.B.R. (1966)
	albumin	<i>Al</i>	<i>F, S</i>	BRAEND and EFREMOV (1965)
	alkaline phosphatase	..	..	RENDEL and STORMONT (1964)
	A esterase	<i>Es</i>	<i>a, b, c</i>	LEE (1966); TUCKER <i>et al.</i> (1966)

TABLE 1—Continued

Published locus and gene symbols in current use for protein polymorphisms in certain species of livestock

Species	System name	Locus symbol	Gene symbols	Literature reference
<i>Sus scrofa</i>	transferrin	<i>Tf</i>	<i>A, B</i> <i>C</i>	KRISTANSSON (1960) KING (1962)
	pre-albumin	<i>Pa</i>	<i>A, B</i>	KRISTJANSSON (1963)
	albumin ¹	<i>Alb</i> ₁	<i>A, B, O</i>	KRISTJANSSON (1966)
	haptoglobin	<i>Hp</i>	<i>1, 2, 3</i>	KRISTJANSSON (1961)
			<i>0</i>	BRUMMERSTEDT-HANSEN and HESSELHOLT (1962)
	amylase	<i>T</i>	<i>A, B</i> }	ASHTON (1960)
		<i>Am</i>	<i>1, 2, 3</i> }*	KING (1963); GRAETZER, HESSELHOLT and MOUSTGAARD (1964)
	ceruloplasmin	<i>Cp</i>	<i>a, b</i>	IMLAH (1964)
	Sa ₂ globulin	<i>Sa</i> ₂	<i>A, B, C</i>	SCHRÖPFEL (1965)
<i>Equus caballus</i>	haemoglobin	<i>Hb</i>	<i>A, B</i>	SCHMID (1966)
	transferrin	<i>Tf</i>	<i>D, H, M, O, R</i>	BRAEND and STORMONT (1964)
			<i>F1, F2</i>	GAHNE (1966)
	albumin	<i>a</i>	<i>A, B</i> }	STORMONT and SUZUKI (1963)
		<i>Al</i>	<i>F, S</i> }*	BRAEND (1964)
	pre-albumin	<i>Pr</i>	<i>F, I, L, S</i>	GAHNE (1966)
<i>Gallus domesticus</i>	esterase	<i>Es</i>	<i>F, I, S</i>	GAHNE (1966)
	transferrin	<i>Tf</i>	<i>a, b</i>	OGDEN <i>et al.</i> (1962)
	albumin	<i>Alb</i>	<i>F, S</i>	MCINDOE (1962)
	alkaline phosphatase	<i>Ap</i>	<i>2, 4</i>	LAW and MUNRO (1965)
	egg albumen	<i>Ov</i>	<i>A, B</i>	LUSH (1964)
	egg albumen	<i>II</i>	<i>A, B</i>	LUSH (1961)
<i>Capra hircus</i>	egg albumen	<i>III</i>	<i>A, B</i>	LUSH (1961)
	haemoglobin	<i>Hb</i>	<i>A, B</i>	KHANOLKAR <i>et al.</i> (1963)
	transferrin	<i>Tf</i>	<i>A, B</i>	ASHTON and McDUGALL (1958)

* Alternative nomenclatures for same system.

defined by a unique animal or its progeny. Our recommendations for reference samples therefore depend on whether or not the system exhibits codominance.

1. *Systems with codominant alleles*, in which each gene product is fully expressed and there are no hybrid products.

- Only animals which are known to be heterozygous at the locus concerned should be used to provide reference samples. This avoids the possibility of demonstrating heterozygosity in phenotypes thought to represent homozygotes.
- There can be only *one* primary reference animal for any allele, and this animal should act as reference for only one of the two alleles represented at that locus. In the event that the animal becomes unavailable, an animal in its direct line of descent carrying that allele becomes the new reference source.

- c. A given reference sample should be obtained from *one* animal in an established research herd, flock, etc. in which pedigree relationships are accurately recorded.
2. *Noncodominant systems.*
 - a. For systems in which a phenotype may represent a homozygote or heterozygote the reference animal chosen should be a heterozygote (checked by pedigree studies).
 - b. For systems in which the heterozygote shows interaction products not present in either homozygote reference samples of all genotypes should be available for comparison.
 - c. In either case, the principle that there is only one primary reference animal for a given allele should be adhered to.

Arrangements have been made to establish two banks of reference samples, one in Wageningen (Dr. J. Bouw, Duivendaal 5, Wageningen, The Netherlands) and one in Beltsville (Dr. C. A. Kiddy, U.S. Department of Agriculture, Agricultural Research Service, Animal Husbandry Research Division, Beltsville, Maryland 20705, U.S.A.). As far as possible, reference animals will be located in areas of the world where endemic diseases of a transmissible nature are minimal, so that quarantine restrictions imposed by some countries may be met more readily.

CONCLUSION

It is in the best interests of workers in this rapidly expanding field of research that uniformity of nomenclature be achieved as soon as possible. It is the hope of this Committee that the recommendations listed above will meet with general approval and be adopted. We will individually welcome comments on these proposals.

SUMMARY

This report presents the proposals of a Committee appointed by the F.A.O. Expert Panel of Blood Group Scientists to consider the problem of inconsistent nomenclature of protein polymorphisms in farm livestock. Recommendations for nomenclature of loci, alleles, genotypes and phenotypes are given, as well as suggestions for the naming of newly discovered phenotypes in established and newly discovered systems. Proposals to establish two reference sample banks are outlined. These reference samples will originate from single animals, heterozygous for the factor defined, so that the definition will be unique, at least in codominant genetic systems.

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