Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB)

Enzyme Nomenclature

Classification and Nomenclature of Enzymes by the Reactions they Catalyse

1. General principles

Because of their close interdependence, it is convenient to deal with the classification and nomenclature together.

The *first general principle* of these 'Recommendations' is that names purporting to be names of enzymes, especially those ending in *-ase*, should be used only for single enzymes, *i.e.* single catalytic entities. They should not be applied to systems containing more than one enzyme. When it is desired to name such a system on the basis of the overall reaction catalysed by it, the word *system* should be included in the name. For example, the system catalysing the oxidation of succinate by molecular oxygen, consisting of succinate dehydrogenase, cytochrome oxidase, and several intermediate carriers, should not be named *succinate oxidase*, but it may be called the *succinate oxidase system.* Other examples of systems consisting of several structurally and functionally linked enzymes (and cofactors) are the *pyruvate dehydrogenase system*, the similar *2-oxoglutarate dehydrogenase system*, and the *fatty acid synthase system.*

In this context it is appropriate to express disapproval of a loose and misleading practice that is found in the biological literature. It consists in designation of a natural substance (or even of an hypothetical active principle), responsible for a physiological or biophysical phenomenon that cannot be described in terms of a definite chemical reaction, by the name of the phenomenon in conjugation with the suffix *-ase*, which implies an individual enzyme. Some examples of such *phenomenase* nomenclature, which should be discouraged even if there are reasons to suppose that the particular agent may have enzymic properties, are: *permease, translocase, reparase, joinase, replicase, codase, etc.*.

The *second general principle* is that enzymes are principally classified and named according to the reaction they catalyse. The chemical reaction catalysed is the specific property that distinguishes one enzyme from another, and it is logical to use it as the basis for the classification and naming of enzymes.

Several alternative bases for classification and naming had been considered, *e.g.* chemical nature of the enzymes (whether it is a flavoprotein, a hemoprotein, a pyridoxal-phosphate protein, a copper protein, and so on), or chemical nature of the substrate (nucleotides, carbohydrates, proteins, *etc.*). The first cannot serve as a general basis, for only a minority of enzymes have such identifiable prosthetic groups. The chemical nature of the enzyme has, however, been used exceptionally in certain cases where classification based on specificity is difficult, for example, with the peptidases (subclass EC 3.4). The second basis for classification is hardly practicable, owing to the great variety of substances acted upon and because it is not sufficiently informative unless the type of reaction is also given. It is the overall reaction, as expressed by the formal equation, that should be taken as the basis. Thus, the intimate mechanism of the reaction, and the formation of intermediate complexes of the reactants with the enzyme is not taken into account, but only the observed chemical change produced by the complete enzyme reaction. For example, in those cases in which the enzyme contains a prosthetic group that serves to catalyse transfer from a donor to an acceptor (*e.g.* flavin, biotin, or pyridoxal-phosphate enzymes) the name of the prosthetic group is not normally included in the name of the enzyme. Nevertheless, where alternative names are possible, the mechanism may be taken into account in choosing between them.

A consequence of the adoption of the chemical reaction as the basis for naming enzymes is that a systematic name cannot be given to an enzyme until it is known what chemical reaction it catalyses. This applies, for example, to a few enzymes that have so far not been shown to catalyse any chemical reaction, but only isotopic exchanges; the isotopic exchange gives some idea of one step in the overall chemical reaction, but the reaction as a whole remains unknown.

A second consequence of this concept is that a certain name designates not a single enzyme protein but a group of proteins with the same catalytic property. Enzymes from different sources (various bacterial, plant or animal species) are classified as one entry. The same applies to isoenzymes (see below). However, there are exceptions to this general rule. Some are justified because the mechanism of the reaction or the substrate specificity is so different as to warrant different entries in the enzyme list. This applies, for example, to the two cholinesterases, EC 3.1.1.7 and 3.1.1.8, the two citrate hydro-lyases, EC 4.2.1.3 and 4.2.1.4, and the two amine oxidases, EC 1.4.3.4 and 1.4.3.6. Others are mainly historical, *e.g.* acid and alkaline phosphatases (EC 3.1.3.1 and EC 3.1.3.2).

A *third general principle* adopted is that the enzymes are divided into groups on the basis of the type of reaction catalysed, and this, together with the name(s) of the substrate(s) provides a basis for naming individual enzymes. It is also the basis for classification and code numbers.

Special problems attend the classification and naming of enzymes catalysing complicated transformations that can be resolved into several sequential or coupled intermediary reactions of different types, all catalysed by a single enzyme (not an enzyme system). Some of the steps may be spontaneous non-catalytic reactions, while one or more intermediate steps depend on catalysis by the enzyme. Wherever the nature and sequence of intermediary reactions is known or can be presumed with confidence, classification and naming of the enzyme should be based on the first enzyme-catalysed step that is essential to the subsequent transformations, which can be indicated by a supplementary term in parentheses, *e.g. acetyl-CoA:glyoxylate C-acetyltransferase (thioester-hydrolysing, carboxymethyl-forming)* (EC 2.3.3.9, *cf.* section 3).

To classify an enzyme according to the type of reaction catalysed, it is occasionally necessary to choose between alternative ways of regarding a given reaction. Some considerations of this type are outlined in section 3 of this chapter. In general, that alternative should be selected which fits in best with the general system of classification and reduces the number of exceptions.

One important extension of this principle is the question of the direction in which the reaction is written for the purposes of classification. To simplify the classification, the direction chosen should be the same for all enzymes in a given class, even if this direction has not been demonstrated for all. Thus the *systematic* names, on which the classification and code numbers are based, may be derived from a written reaction, even though only the reverse of this has been actually demonstrated experimentally. In the list in this volume, the reaction is written to illustrate the classification, *i.e.* in the direction described by the systematic name. However, the *common* name may be based on either direction of reaction, and is often based on the presumed physiological direction.

Many examples of this usage are found in section 1 of the list. The reaction for EC 1.1.1.9 is written as an oxidation of xylitol by NAD^+, in parallel with all other oxidoreductases in subgroup EC 1.1.1, and the systematic name is accordingly, *xylitol:NAD^+ 2-oxidoreductase (*D-*xylulose-forming)*. However, the common name, based on the reverse direction of reaction, is D-*xylulose reductase*.

2. Common and Systematic Names

The first Enzyme Commission gave much thought to the question of a systematic and logical nomenclature for enzymes, and finally recommended that there should be two nomenclatures for enzymes, one systematic, and one working or trivial. The systematic name of an enzyme, formed in accordance with definite rules,

showed the action of an enzyme as exactly as possible, thus identifying the enzyme precisely. The trivial name was sufficiently short for general use, but not necessarily very systematic; in a great many cases it was a name already in current use. The introduction of (often cumbersome) systematic names was strongly criticised. In many cases the reaction catalysed is not much longer than the systematic name and can serve just as well for identification, especially in conjunction with the code number.

The Commission for Revision of Enzyme Nomenclature discussed this problem at length, and a change in emphasis was made. It was decided to give the trivial names more prominence in the Enzyme List; they now follow immediately after the code number, and are described as Common Name. Also, in the index the common names are indicated by an asterisk. Nevertheless, it was decided to retain the systematic names as the basis for classification for the following reasons:

(i) the code number alone is only useful for identification of an enzyme when a copy of the Enzyme List is at hand, whereas the systematic name is self-explanatory;

(ii) the systematic name stresses the type of reaction, the reaction equation does not;

(iii) systematic names can be formed for new enzymes by the discoverer, by application of the rules, but code numbers should **not** be assigned by individuals;

(iv) common names for new enzymes are frequently formed as a condensed version of the systematic name; therefore, the systematic names are helpful in finding common names that are in accordance with the general pattern.

It is recommended that for enzymes that are not the main subject of a paper or abstract, the common names should be used, but they should be identified at their first mention by their code numbers and source. Where an enzyme is the main subject of a paper or abstract, its code number, systematic name, or, alternatively, the reaction equation and source should be given at its first mention; thereafter the common name should be used. In the light of the fact that enzyme names and code numbers refer to reactions catalysed rather than to discrete proteins, it is of special importance to give also the source of the enzyme for full identification; in cases where multiple forms are known to exist, knowledge of this should be included where available.

When a paper deals with an enzyme that is not yet in the Enzyme List, the author may introduce a new name and, if desired, a new systematic name, both formed according to the recommended rules. A number should be assigned only by the Nomenclature Committee of IUBMB.

The Enzyme List contains one or more references for each enzyme. It should be stressed that no attempt has been made to provide a complete bibliography, or to refer to the first description of an enzyme. The references are intended to provide sufficient evidence for the existence of an enzyme catalysing the reaction as set out. Where there is a major paper describing the purification and specificity of an enzyme, or a major review article, this has been quoted to the exclusion of earlier and later papers. In some cases separate references are given for animal, plant and bacterial enzymes.

3. Scheme for the classification of enzymes and the generation of EC numbers

The first Enzyme Commission, in its report in 1961, devised a system for classification of enzymes that also serves as a basis for assigning code numbers to them. These code numbers, prefixed by EC, which are now widely in use, contain four elements separated by points, with the following meaning:

(i) the first number shows to which of the six main divisions (classes) the enzyme belongs,

(ii) the second figure indicates the subclass,

(iii) the third figure gives the sub-subclass,

(iv) the fourth figure is the serial number of the enzyme in its sub-subclass.

The subclasses and sub-subclasses are formed according to principles indicated below.

The main divisions and subclasses are:

Class 1. Oxidoreductases.

To this class belong all enzymes catalysing oxidoreduction reactions. The substrate that is oxidized is regarded as hydrogen donor. The systematic name is based on *donor:acceptor oxidoreductase*. The common name will be *dehydrogenase*, wherever this is possible; as an alternative, *reductase* can be used. *Oxidase* is only used in cases where O_2 is the acceptor.

The second figure in the code number of the oxidoreductases, unless it is 11, 13, 14 or 15, indicates the group in the hydrogen (or electron) donor that undergoes oxidation: 1 denotes a -CHOH- group, 2 a -CHO or -CO-COOH group or carbon monoxide, and so on, as listed in the key.

The third figure, except in subclasses EC 1.11, EC 1.13, EC 1.14 and EC 1.15, indicates the type of acceptor involved: 1 denotes $NAD(P)^+$, 2 a cytochrome, 3 molecular oxygen, 4 a disulfide, 5 a quinone or similar compound, 6 a nitrogenous group, 7 an iron-sulfur protein and 8 a flavin. In subclasses EC 1.13 and EC 1.14 a different classification scheme is used and sub-subclasses are numbered from 11 onwards.

It should be noted that in reactions with a nicotinamide coenzyme this is always regarded as acceptor, even if this direction of the reaction is not readily demonstrated. The only exception is the subclass EC 1.6, in which NAD(P)H is the donor; some other redox catalyst is the acceptor.

Although not used as a criterion for classification, the two hydrogen atoms at carbon-4 of the dihydropyridine ring of nicotinamide nucleotides are not equivalent in that the hydrogen is transferred stereospecifically.

Class 2. Transferases.

Transferases are enzymes transferring a group, *e.g.* a methyl group or a glycosyl group, from one compound (generally regarded as donor) to another compound (generally regarded as acceptor). The systematic names are formed according to the scheme *donor:acceptor grouptransferase*. The common names are normally formed according to *acceptor grouptransferase* or *donor grouptransferase*. In many cases, the donor is a cofactor (coenzyme) charged with the group to be transferred. A special case is that of the transaminases (see below).

Some transferase reactions can be viewed in different ways. For example, the enzyme-catalysed reaction

$$X\text{-}Y + Z = X + Z\text{-}Y$$

may be regarded either as a transfer of the group Y from X to Z, or as a breaking of the X-Y bond by the introduction of Z. Where Z represents phosphate or arsenate, the process is often spoken of as 'phosphorolysis' or 'arsenolysis', respectively, and a number of enzyme names based on the pattern of *phosphorylase* have come into use. These names are not suitable for a systematic nomenclature, because there is no reason to single out these particular enzymes from the other transferases, and it is better to regard them simply as *Y-transferases*.

In the above reaction, the group transferred is usually exchanged, at least formally, for hydrogen, so that the equation could more strictly be written as:

$$X\text{-}Y + Z\text{-}H = X\text{-}H + Z\text{-}Y.$$

Another problem is posed in enzyme-catalysed transaminations, where the $-NH_2$ group and -H are transferred to a compound containing a carbonyl group in exchange for the =O of that group, according to the general equation:

$$R^1\text{-}CH(\text{-}NH_2)\text{-}R^2 + R^3\text{-}CO\text{-}R^4 \rightarrow R^1\text{-}CO\text{-}R^2 + R^3\text{-}CH(\text{-}NH_2)\text{-}R^4.$$

The reaction can be considered formally as oxidative deamination of the donor (*e.g.* amino acid) linked with reductive amination of the acceptor (*e.g.* oxo acid), and the transaminating enzymes (pyridoxal-phosphate proteins) might be classified as oxidoreductases. However, the unique distinctive feature of the reaction is the transfer of the amino group (by a well-established mechanism involving covalent substrate-coenzyme intermediates), which justified allocation of these enzymes among the transferases as a special subclass (EC 2.6.1, *transaminases*).

The second figure in the code number of transferases indicates the group transferred; a one-carbon group in EC 2.1, an aldehydic or ketonic group in EC 2.2, an acyl group in EC 2.3 and so on.

The third figure gives further information on the group transferred; *e.g.* subclass EC 2.1 is subdivided into *methyltransferases* (EC 2.1.1), *hydroxymethyl-* and *formyltransferases* (EC 2.1.2) and so on; only in subclass EC 2.7, does the third figure indicate the nature of the acceptor group.

Class 3. Hydrolases.

These enzymes catalyse the hydrolytic cleavage of C-O, C-N, C-C and some other bonds, including phosphoric anhydride bonds. Although the systematic name always includes *hydrolase*, the common name is, in many cases, formed by the name of the substrate with the suffix *-ase*. It is understood that the name of the substrate with this suffix means a hydrolytic enzyme.

A number of hydrolases acting on ester, glycosyl, peptide, amide or other bonds are known to catalyse not only hydrolytic removal of a particular group from their substrates, but likewise the transfer of this group to suitable acceptor molecules. In principle, all hydrolytic enzymes might be classified as transferases, since hydrolysis itself can be regarded as transfer of a specific group to water as the acceptor. Yet, in most cases, the reaction with water as the acceptor was discovered earlier and is considered as the main physiological function of the enzyme. This is why such enzymes are classified as hydrolases rather than as transferases.

Some hydrolases (especially some of the esterases and glycosidases) pose problems because they have a very wide specificity and it is not easy to decide if two preparations described by different authors (perhaps from different sources) have the same catalytic properties, or if they should be listed under separate entries. An example is *vitamin A esterase* (formerly EC 3.1.1.12, now believed to be identical with EC 3.1.1.1). To some extent the choice must be arbitrary; however, separate entries should be given only when the specificities are sufficiently different.

Another problem is that proteinases have 'esterolytic' action; they usually hydrolyse ester bonds in appropriate substrates even more rapidly than natural peptide bonds. In this case, classification among the peptide hydrolases is based on historical priority and presumed physiological function.

The second figure in the code number of the hydrolases indicates the nature of the bond hydrolysed; EC 3.1 are the *esterases*; EC 3.2 the *glycosylases*, and so on.

The third figure normally specifies the nature of the substrate, *e.g.* in the esterases the *carboxylic ester hydrolases* (EC 3.1.1), *thiolester hydrolases* (EC 3.1.2), *phosphoric monoester hydrolases* (EC 3.1.3); in the glycosylases the *O-glycosidases* (EC 3.2.1), *N-glycosylases* (EC 3.2.2), *etc*. Exceptionally, in the case of the

peptidyl-peptide hydrolases the third figure is based on the catalytic mechanism as shown by active centre studies or the effect of pH.

Class 4. Lyases.

Lyases are enzymes cleaving C-C, C-O, C-N, and other bonds by elimination, leaving double bonds or rings, or conversely adding groups to double bonds. The systematic name is formed according to the pattern *substrate group-lyase*. The hyphen is an important part of the name, and to avoid confusion should not be omitted, *e.g. hydro-lyase* not 'hydrolyase'. In the common names, expressions like *decarboxylase, aldolase, dehydratase* (in case of elimination of CO_2, aldehyde, or water) are used. In cases where the reverse reaction is much more important, or the only one demonstrated, *synthase* (not synthetase) may be used in the name. Various subclasses of the lyases include pyridoxal-phosphate enzymes that catalyse the elimination of a b- or g-substituent from an a-amino acid followed by a replacement of this substituent by some other group. In the overall replacement reaction, no unsaturated end-product is formed; therefore, these enzymes might formally be classified as *alkyl-transferases* (EC 2.5.1...). However, there is ample evidence that the replacement is a two-step reaction involving the transient formation of enzyme-bound a,b(or b,g)-unsaturated amino acids. According to the rule that the first reaction is indicative for classification, these enzymes are correctly classified as *lyases*. Examples are *tryptophan synthase* (EC 4.2.1.20) and *cystathionine b-synthase* (EC 4.2.1.22).

The second figure in the code number indicates the bond broken: EC 4.1 are carbon-carbon lyases, EC 4.2 carbon-oxygen lyases and so on.

The third figure gives further information on the group eliminated (*e.g.* CO_2 in EC 4.1.1, H_2O in EC 4.2.1).

Class 5. Isomerases.

These enzymes catalyse geometric or structural changes within one molecule. According to the type of isomerism, they may be called *racemases, epimerases, cis-trans-isomerases, isomerases, tautomerases, mutases* or *cycloisomerases*.

In some cases, the interconversion in the substrate is brought about by an intramolecular oxidoreduction (EC 5.3); since hydrogen donor and acceptor are the same molecule, and no oxidized product appears, they are not classified as oxidoreductases, even though they may contain firmly bound $NAD(P)^+$.

The subclasses are formed according to the type of isomerism, the sub-subclasses to the type of substrates.

Class 6. Ligases.

Ligases are enzymes catalysing the joining together of two molecules coupled with the hydrolysis of a diphosphate bond in ATP or a similar triphosphate. The systematic names are formed on the system *X:Y ligase (ADP-forming).* In earlier editions of the list the term *synthetase* has been used for the common names. Many authors have been confused by the use of the terms *synthetase* (used only for Group 6) and *synthase* (used throughout the list when it is desired to emphasis the synthetic nature of the reaction). Consequently NC-IUB decided in 1983 to abandon the use of synthetase for common names, and to replace them with names of the type *X-Y ligase*. In a few cases in Group 6, where the reaction is more complex or there is a common name for the product, a synthase name is used (*e.g.* EC 6.3.2.11 and EC 6.3.5.1).

It is recommended that if the term *synthetase* is used by authors, it should continue to be restricted to the ligase group.

The second figure in the code number indicates the bond formed: EC 6.1 for C-O bonds (enzymes acylating

tRNA), EC 6.2 for C-S bonds (acyl-CoA derivatives), *etc.* Sub-subclasses are only in use in the C-N ligases.

In a few cases it is necessary to use the word *other* in the description of subclasses and sub-subclasses. They have been provisionally given the figure 99, in order to leave space for new subdivisions.

From time to time, some enzymes have been deleted from the List, while some others have been renumbered. However, the old numbers have ***not*** been allotted to new enzymes; rather the place has been left vacant and cross-reference is made according to the following scheme:

[**EC 1.2.3.4 Deleted entry:** old name]

or

[**EC 1.2.3.4 Transferred entry:** now EC 5.6.7.8 - common name].

Entries for reclassified enzymes transferred from one position in the List to another are followed, for reference, by a comment indicating the former number.

It is regarded as important that the same policy be followed in future revisions and extensions of the Enzyme List, which may become necessary from time to time.

4. Rules for Classification and Nomenclature

(a) General Rules for Systematic Names and Guidelines for Common Names

Rule 1.

(Common Names)

Generally accepted trivial names of substrates may be used in enzyme names. The prefix D- should be omitted for all D-sugars and L- for individual amino acids, unless ambiguity would be caused. In general, it is not necessary to indicate positions of substituents in common names, unless it is necessary to prevent two different enzymes having the same name. The prefix *keto* is no longer used for derivatives of sugars in which -CHOH- has been replaced by -CO-; they are named throughout as dehydro-sugars.

(Systematic Names)

To produce usable systematic names, accepted trivial names of substrates forming part of the enzyme names should be used. Where no accepted and convenient trivial names exist, the official IUPAC rules of nomenclature should be applied to the substrate name. The 1,2,3 system of locating substituents should be used instead of the a,b,g system, although group names such as b-aspartyl-, g-glutamyl-, and also b-alanine and g-lactone are permissible; a,b should normally be used for indicating configuration, as in a-D-glucose. For nucleotide groups, *adenylyl* (not adenyl), *etc*. should be the form used. The name oxo acids (not keto acids) may be used as a class name, and for individual compounds in which $-CH_2-$ has been replaced by -CO-, oxo should be used.

Rule 2.

Where the substrate is normally in the form of an anion, its name should end in *-ate* rather than *-ic; e.g. lactate dehydrogenase*, not 'lactic dehydrogenase' or 'lactic acid dehydrogenase'.

Rule 3.

Commonly used abbreviations for substrates, *e.g.* ATP, may be used in names of enzymes, but the use of new abbreviations (not listed in recommendations of the IUPAC-IUB Commission on Biochemical Nomenclature) should be discouraged. Chemical formulae should not normally be used instead of names of substrates. Abbreviations for names of enzymes, *e.g.* GDH, should not be used.

Rule 4.

Names of substrates composed of two nouns, such as glucose phosphate, which are normally written with a space, should be hyphenated when they form part of the enzyme names, and thus become adjectives, *e.g. glucose-6-phosphate 1-dehydrogenase* (EC 1.1.1.49). This follows standard practice in phrases where two nouns qualify a third; see, for example, *Handbook for Chemical Society Authors*, 2nd edn, p. 14 (The Chemical Society, London, 1961).

Rule 5.

The use as enzyme names of descriptions such as *condensing enzyme, acetate-activating enzyme, pH 5 enzyme* should be discontinued as soon as the catalysed reaction is known. The word *activating* should not be used in the sense of converting the substrate into a substance that reacts further; all enzymes act by activating their substrates, and the use of the word in this sense may lead to confusion.

Rule 6.

(Common Names)

If it can be avoided, a common name should not be based on a substance that is not a true substrate, *e.g.* enzyme EC 4.2.1.17 should not be called 'crotonase', since it does not act on crotonate.

Rule 7.

(Common Names)

Where a name in common use gives some indication of the reaction and is not incorrect or ambiguous, its continued use is recommended. In other cases a common name is based on the same general principles as the systematic name (see Rule 7 below) but with a minimum of detail, to produce a name short enough for convenient use. A few names of proteolytic enzymes ending in *-in* are retained; all other enzyme names should end in *-ase*.

(Systematic Names)

Systematic names consist of two parts. The first contains the name of the substrate or, in the case of a bimolecular reaction, of the two substrates separated by a colon. The second part, ending in *-ase*, indicates the nature of the reaction.

Rule 8.

A number of generic words indicating a type of reaction may be used in either common or systematic names: *oxidoreductase, oxygenase, transferase* (with a prefix indicating the nature of the group transferred), *hydrolase, lyase, racemase, epimerase, isomerase, mutase, ligase.*

Rule 9.

(Common Names)

A number of additional generic words indicating reaction types are used in common names, but not in the

systematic nomenclature, *e.g. dehydrogenase, reductase, oxidase, peroxidase, kinase, tautomerase, deaminase, dehydratase, etc.*.

Rule 10.

Where additional information is needed to make the reaction clear, a phrase indicating the reaction or a product should be added in parentheses after the second part of the name *e.g. (ADP-forming), (dimerizing), (CoA-acylating).*

Rule 11.

(Common Names)

The direct attachment of *-ase* to the name of the substrate will indicate that the enzyme brings about hydrolysis.

(Systematic Names)

The suffix *-ase* should never be attached directly to the name of the substrate.

Rule 12.

(Common Names)

The name 'dehydrase' which was at one time used for both dehydrogenating and dehydrating enzymes, should not be used. *Dehydrogenase* will be used for the former and *dehydratase* for the latter.

Rule 13.

(Common Names)

Where possible, common names should normally be based on a reaction direction that has been demonstrated, *e.g. dehydrogenase* or *reductase, decarboxylase* or *carboxylase*.

(Systematic Names)

In the case of reversible reactions, the direction chosen for naming should be the same for all the enzymes in a given class, even if this direction has not been demonstrated for all. Thus, systematic names may be based on a written reaction, even though only the reverse of this has been actually demonstrated experimentally.

Rule 14.

(Systematic Names)

When the overall reaction includes two different changes, *e.g.* an oxidative demethylation, the classification and systematic name should be based, whenever possible, on the one (or the first one) catalysed by the enzyme; the other function(s) should be indicated by adding a suitable participle in parentheses, as in the case of *sarcosine:oxygen oxidoreductase (demethylating)* (EC 1.5.3.1); D-*aspartate:oxygen oxidoreductase (deaminating)* (EC 1.4.3.1); L-*serine hydro-lyase (adding indoleglycerol-phosphate)* (EC 4.2.1.20).

Other examples of such additions are *(decarboxylating), (cyclizing), (acceptor-acylating), (isomerizing).*

Rule 15.

When an enzyme catalyses more than one type of reaction, the name should normally refer to one reaction only. Each case must be considered on its merits, and the choice must be, to some extent, arbitrary. Other important activities of the enzyme may be indicated in the List under 'Reaction' or 'Comments'.

Similarly, when any enzyme acts on more than one substrate (or pair of substrates), the name should normally refer only to one substrate (or pair of substrates), although in certain cases it may be possible to use a term that covers a whole group of substrates, or an alternative substrate may be given in parentheses.

Rule 16.

A group of enzymes with closely similar specificities should normally be described by a single entry. However, when the specificity of two enzymes catalysing the same reactions is sufficiently different (the degree of difference being a matter of arbitrary choice) two separate entries may be made, *e.g.* EC 1.2.1.4 and EC 1.2.1.7. Separate entries are also appropriate for enzymes having similar catalytic functions, but known to differ basically with regard to reaction mechanism or to the nature of the catalytic groups, *e.g. amine oxidase (flavin-containing)* (EC 1.4.3.4) and *amine oxidase (copper-containing)* (EC 1.4.3.6).

(b) Rules and Guidelines for Particular Classes of Enzymes

Class 1

Rule 17.

(Common Names)

The terms *dehydrogenase* or *reductase* will be used much as hitherto. The latter term is appropriate when hydrogen transfer from the substance mentioned as donor in the systematic name is not readily demonstrated. *Transhydrogenase* may be retained for a few well-established cases. *Oxidase* is used only for cases there O_2 acts as an acceptor, and *oxygenase* only for those cases where the O_2 molecule (or part of it) is directly incorporated into the substrate. *Peroxidase* is used for enzymes using H_2O_2 as acceptor. *Catalase* must be regarded as exceptional. Where no ambiguity is caused, the second reactant is not usually named; but where required to prevent ambiguity, it may be given in parentheses, *e.g.* EC 1.1.1.1, *alcohol dehydrogenase* and EC 1.1.1.2, *alcohol dehydrogenase ($NADP^+$)*.

(Systematic Names)

All enzymes catalysing oxidoreductions should be named *oxidoreductases* in the systematic nomenclature, and the names formed on the pattern *donor:acceptor oxidoreductase*.

Rule 18.

(Systematic Names)

For oxidoreductases using NAD^+ or $NADP^+$, the coenzyme should always be named as the acceptor except for the special case of Section 1.6 (enzymes whose normal physiological function is regarded as reoxidation of the reduced coenzyme). Where the enzyme can use either coenzyme, this should be indicated by writing $NAD(P)^+$.

Rule 19.

Where the true acceptor is unknown and the oxidoreductase has only been shown to react with artificial acceptors, the word *acceptor* should be written in parentheses, as in the case of EC 1.3.99.1, *succinate: (acceptor) oxidoreductase*.

Rule 20.

(Common Names)

Oxidoreductases that bring about the incorporation of molecular oxygen into one donor or into either or both of a pair of donors are named *oxygenase*. If only one atom of oxygen is incorporated the term *monooxygenase* is used; if both atoms of O_2 are incorporated, the term *dioxygenase* is used.

(Systematic Names)

Oxidoreductases bringing about the incorporation of oxygen into one of paired donors should be named on the pattern *donor,donor:oxygen oxidoreductase (hydroxylating).*

Class 2.

Rule 21.

(Common Names)

Only one specific substrate or reaction product is generally indicated in the common names, together with the group donated or accepted.

The forms *transaminase, etc.*, may be replaced if desired by the corresponding forms *aminotransferase, etc.*.

A number of special words are used to indicate reaction types, *e.g. kinase* to indicate a phosphate transfer from ATP to the named substrate (not 'phosphokinase'), *diphosphokinase* for a similar transfer of diphosphate.

(Systematic Names)

Enzymes catalysing group-transfer reactions should be named *transferase* and the names formed on the pattern *donor:acceptor group-transferred-transferase, e.g. ATP:acetate phosphotransferase* (EC 2.7.2.1). A figure may be prefixed to show the position to which the group is transferred, *e.g. ATP:*D-*fructose 1-phosphotransferase* (EC 2.7.1.3). The spelling 'transphorase' should not be used. In the case of the phosphotransferases, ATP should always be named as the donor. In the case of the transaminases involving 2-oxoglutarate, the latter should always be named as the acceptor.

Rule 22.

(Systematic Names)

The prefix denoting the group transferred should, as far as possible, be non-committal with respect to the mechanism of the transfer, *e.g. phospho-*, rather than *phosphate-*.

Class 3.

Rule 23.

(Common Names)

The direct addition of *-ase* to the name of the substrate generally denotes a hydrolase. Where this is difficult, *e.g.* for EC 3.1.2.1, the word *hydrolase* may be used. Enzymes should not normally be given separate names merely on the basis of optimal conditions for activity. The acid and alkaline phosphatases (EC 3.1.3.1-2) should be regarded as special cases and not as examples to be followed. The common name *lysozyme* is also

exceptional.

(Systematic Names)

Hydrolysing enzymes should be systematically named on the pattern *substrate hydrolase*. Where the enzyme is specific for the removal of a particular group, the group may be named as a prefix, *e.g. adenosine aminohydrolase* (EC 3.5.4.4). In a number of cases this group can also be transferred by the enzyme to other molecules, and the hydrolysis itself might be regarded as a transfer of the group to water.

Class 4.

Rule 24.

(Common Names)

The old names *decarboxylase, aldolase, etc.*, are retained; and *dehydratase* (not 'dehydrase') is used for the hydro-lyases. 'Synthetase' should not be used for any enzymes in this class. The term *synthase* may be used instead for any enzyme in this class (or any other class) when it is desired to emphasize the synthetic aspect of the reaction.

(Systematic Names)

Enzymes removing groups from substrates non-hydrolytically, leaving double bonds (or adding groups to double bonds) should be called *lyases* in the systematic nomenclature. Prefixes such as *hydro-, ammonia-* should be used to denote the type of reaction, *e.g. (*S*)-malate hydro-lyase* (EC 4.2.1.2). Decarboxylases should be regarded as *carboxy-lyases*. A hyphen should always be written before *lyase* to avoid confusion with hydrolases, carboxylases, *etc*.

Rule 25.

(Common Names)

Where the equilibrium warrants it, or where the enzyme has long been named after a particular substrate, the reverse reaction may be taken as the basis of the name, using *hydratase, carboxylase, etc., e.g. fumarate hydratase* for EC 4.2.1.2 (in preference to 'fumarase', which suggests an enzyme hydrolysing fumarate).

(Systematic Names)

The complete molecule, not either of the parts into which it is separated, should be named as the substrate.

The part indicated as a prefix to *-lyase* is the more characteristic and usually, but not always, the smaller of the two reaction products. This may either be the removed (saturated) fragment of the substrate molecule, as in *ammonia-, hydro-, thiol-lyases, etc*. or the remaining unsaturated fragment, *e.g.* in the case of *carboxy-, aldehyde-* or *oxo-acid-lyases*.

Rule 26.

Various subclasses of the lyases include a number of strictly specific or group-specific pyridoxal-5-phosphate enzymes that catalyse *elimination* reactions of b- or g-substituted a-amino acids. Some closely related pyridoxal-5-phosphate-containing enzymes, *e.g. tryptophan synthase* (EC 4.2.1.20) and *cystathionine* b-*synthase* (EC 4.2.1.22) catalyse *replacement* reactions in which a b- or g-substituent is replaced by a second reactant without creating a double bond. Formally, these enzymes appear to be transferases rather than lyases. However, there is evidence that in these cases the elimination of the b- or g-substituent and the

formation of an unsaturated intermediate is the first step in the reaction. Thus, applying rule 14, these enzymes are correctly classified as lyases.

Class 5.

Rule 27.

In this class, the common names are, in general, similar to the systematic names which indicate the basis of classification.

Rule 28.

Isomerase will be used as a general name for enzymes in this class. The types of isomerization will be indicated in systematic names by prefixes, *e.g. maleate cis-trans-isomerase* (EC 5.2.1.1), *phenylpyruvate keto-enol-isomerase* (EC 5.3.2.1), *3-oxosteroid* D^5*-* D^4*-isomerase* (EC 5.3.3.1). Enzymes catalysing an aldose-ketose interconversion will be known as *aldose-ketose-isomerases, e.g.* L-*arabinose aldose-ketose-isomerase* (EC 5.3.1.4). When the isomerization consists of an intramolecular transfer of a group, the enzyme is named a *mutase*, *e.g.* EC 5.4.1.1, and the *phosphomutases* in sub-subclass 5.4.2; when it consists of an intramolecular lyase-type reaction, *e.g.* EC 5.5.1.1, it is systematically named a *lyase (decyclizing)*.

Rule 29.

Isomerases catalysing inversions at asymmetric centres should be termed *racemases* or *epimerases*, according to whether the substrate contains one, or more than one, centre of asymmetry: compare, for example, EC 5.1.1.5 with EC 5.1.1.7. A numerical prefix to the word *epimerase* should be used to show the position of the inversion.

Class 6.

Rule 30

(Common Names)

Common names for enzymes of this class were previously of the type *XY synthetase*. However, as this use has not always been understood and synthetase has been confused with synthase (see Rule 24), it is now recommended that as far as possible the common names should be similar in form to the systematic names.

(Systematic Names)

The class of enzymes catalysing the linking together of two molecules, coupled with the breaking of a diphosphate link in ATP, *etc*. should be known as *ligases*. These enzymes were often previously known as 'synthetases'; however, this terminology differs from all other systematic enzyme names in that it is based on the product and not on the substrate. For these reasons, a new systematic class name was necessary.

Rule 31

(Common Names)

The common names should be formed on the pattern *X-Y ligase*, where X-Y is the substance formed by linking X and Y. In certain cases, where a trivial name is commonly used for XY, a name of the type *XY synthase* may be recommended (*e.g.* EC 6.3.2.11, *carnosine synthase*).

(Systematic Names)

The systematic names should be formed on the pattern *X:Y ligase (ADP-forming)*, where X and Y are the two molecules to be joined together. The phrase shown in parentheses indicates both that ATP is the triphosphate involved, and also that the terminal diphosphate link in broken. Thus, the reaction is X + Y + ATP = X-Y + ADP + P_i.

Rule 32.

(Common Names)

In the special case where glutamine acts as an ammonia-donor, this is indicated by adding in parentheses (*glutamine-hydrolysing*) to a ligase name.

(Systematic Names)

In this case, the name *amido-ligase* should be used in the systematic nomenclature.

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