ENZYME NOMENCLATURE

Recommendations (1978)
of the Nomenclature Committee
of the International Union of Biochemistry

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1978

RECOMMENDATIONS OF THE NOMENCLATURE COMMITTEE OF THE INTERNATIONAL UNION OF BIOCHEMISTRY ON THE NOMENCLATURE AND CLASSIFICATION OF ENZYMES

This edition is a revision of the Recommendations (1972) of the IUPAC–IUB Commission on Biochemical Nomenclature, and has been approved for publication by the Executive Committee of the International Union of Biochemistry.

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ABBREVIATIONS USED IN THE ENZYME LIST

The spellings used throughout are those common in Great Britain, but those current in the U.S. may be used instead in recommended names as in the following examples: glycollate, glycolate; sulphur, sulfur; oestradiol, estradiol.

ADP	adenosine 5′-diphosphate
AMP	adenosine 5′-monophosphate
ATP	adenosine 5′-triphosphate
dATP	deoxyadenosine 5′-triphosphate
CDP	cytidine 5′-diphosphate
CMP	cytidine 5′-monophosphate
dCMP	deoxycytidine 5′-monophosphate
CoA	*coenzyme* A
CTP	cytidine 5′-triphosphate
dCTP	deoxycytidine 5′-triphosphate
DFP	diisopropyl fluorophosphate
DNA	deoxyribonucleic acid
FAD	flavin-adenine dinucleotide
FMN	flavin mononucleotide (riboflavin 5′-monophosphate)
GDP	guanosine 5′-diphosphate
dGDP	deoxyguanosine 5′-diphosphate
GMP	guanosine 5′-monophosphate
dGMP	deoxyguanosine 5′-monophosphate
GTP	guanosine 5′-triphosphate
dGTP	deoxyguanosine 5′-triphosphate
IDP	inosine 5′-diphosphate
IMP	inosine 5′-monophosphate
ITP	inosine 5′-triphosphate
NAD^+	oxidized nicotinamide-adenine dinucleotide

NADH	reduced nicotinamide-adenine dinucleotide
$NADP^+$	oxidized nicotinamide-adenine dinucleotide phosphate
$NAD(P)^+$	indicates either NAD^+ or $NADP^+$
NADPH	reduced nicotinamide-adenine dinucleotide phosphate
NAD(P)H	indicates either NADH or NADPH
NDP	nucleoside 5′-diphosphate
NMN	nicotinamide mononucleotide
NMP	nucleoside 5′-monophosphate
dNMP	deoxynucleoside 5′-monophosphate
NTP	nucleoside 5′-triphosphate
P	phosphate residues
poly(C)	synthetic polynucleotide composed of cytidylate residues
poly(G)	synthetic polynucleotide composed of guanylate residues
RNA	ribonucleic acid
tRNA	transfer ribonucleic acid
TDP	ribothymidine 5′-diphosphate
dTDP	thymidine 5′-diphosphate
TMP	ribothymidine 5′-monophosphate
dTMP	thymidine 5′-monophosphate
TTP	ribothymidine 5′-triphosphate
dTTP	thymidine 5′-triphosphate
UDP	uridine 5′-diphosphate
UMP	uridine 5′-monophosphate
dUMP	deoxyuridine 5′-monophosphate
UTP	uridine 5′-triphosphate
dUTP	deoxyuridine 5′-triphosphate

CHAPTER 1

HISTORICAL INTRODUCTION

The rapid growth in the science of enzymology, and the great increase in the number of enzymes known, have given rise to many difficulties of terminology in recent years. By about 1955 it had become evident that the nomenclature of the subject, in the absence of any guiding authority, was getting out of hand. The naming of enzymes by individual workers had proved far from satisfactory in practice. In many cases the same enzymes became known by several different names, while conversely there were cases in which the same name was given to different enzymes. Many of the names conveyed little or no idea of the nature of the reactions catalysed, and similar names were sometimes given to enzymes of quite different types. To meet this situation, various attempts to bring order into the general nomenclature of enzymes, or into that of particular groups of enzymes, were made by individuals or small groups of specialists. But none of the resulting nomenclatures met with general approval.

Furthermore, no general agreement had been reached on the nomenclature of the coenzymes, on which so many names of enzymes inevitably depend; in the equations of enzyme kinetics different systems of mathematical symbols were used by different workers; and the standardization of enzymes was in a chaotic state, owing to the multiplicity of arbitrarily defined units of enzyme activity.

In view of this state of affairs, the General Assembly of the International Union of Biochemistry (IUB) decided, during the third International Congress of Biochemistry in Brussels in August, 1955, to set up an International Commission on Enzymes. This step was taken in consultation with the International Union of Pure and Applied Chemistry (IUPAC).

The International Commission on Enzymes was established in 1956 by the President of the International Union of Biochemistry, Professor M. Florkin, with the advice of an *ad hoc* Committee. The following members were appointed by the Bureau of the International Union of Biochemistry:

> A.E. Braunstein, U.S.S.R.; S.P. Colowick, U.S.A.; P.A.E. Desnuelle, France; M. Dixon, U.K. *(Chairman)*; W.A. Engelhardt, U.S.S.R.; E.F. Gale, U.K.; O. Hoffmann-Ostenhof, Austria; A.L. Lehninger, U.S.A.; K. Linderstrøm-Lang, Denmark; F. Lynen, Germany.
>
> *Corresponding Members*: F. Egami, Japan; L.F. Leloir, Argentina.

In 1959, on the death of K. Linderstrøm-Lang, E.C. Webb (United Kingdom, later Australia) joined the Commission.

The terms of reference of the Enzyme Commission, as laid down by the *ad hoc* Committee, were as follows:

> *'To consider the classification and nomenclature of enzymes and coenzymes, their units of activity and standard methods of assay, together with the symbols used in the description of enzyme kinetics.'*

The Enzyme Commission faced many difficulties arising from the uncontrolled naming of the rapidly increasing number of known enzymes. Some of the names in use were definitely misleading; others conveyed little or nothing about the nature of the reaction catalysed, as for example, ***diaphorase, Zwischenferment, catalase***. Enzymes catalysing essentially similar reaction had sometimes names implying that they belong to different groups, while some enzymes of different types had been placed in the same group, for example, the ***pyrophosphorylases*** had included both glycosyl-transferases and phospho-

transferases. In some cases a name which had been well established for many years with a definite meaning, such as the term ***synthetase***, had been later employed with different meanings, causing confusion.

One of the main tasks given to the Commission was therefore to see how the nomenclature of enzymes could best be brought into a satisfactory state, and whether a code of systematic rules could be devised that would serve as a guide for the consistent naming of new enzymes in the future. At the same time, the Commission realised the difficulties that would be caused by a large number of changes of well-known enzyme names, and the desirability of retaining the existing names wherever there was no good reason for making an alteration. Nevertheless, the overriding consideration was to reduce the confusion and prevent futher confusion from arising. Its task could not have been accomplished without causing some inconvenience, for this was the inevitable result of having allowed the problem to drift for a considerable time.

Throughout its work, the Enzyme Commission was in close touch with the Biological Chemistry Nomenclature Commission of IUPAC. In addition, it considered many comments and suggestions from various experts in the field; 52 formal documents were circulated and discussed in several meetings. Finally, the Commission prepared a report, which was presented to the General Assembly of the International Union of Biochemistry at their meeting in Moscow, 1961, and was adopted. The nomenclature set out in that report has been widely used in scientific journals, textbooks, *etc.* since 1961.

Subsequently, the Council of IUB dissolved the Commission on Enzymes and set up a Standing Committee on Enzymes consisting of S.P. Colowick, O. Hoffmann-Ostenhof, A.L. Lehninger and E.C. Webb *(Secretary)*. This Standing Committee discussed the comments and criticisms received on the published report of the Enzyme Commission and prepared in 1964 a second version, the *Recommendations (1964) of the International Union of Biochemistry on the Nomenclature and Classification of Enzymes.*

The function of the Standing Committee on Enzymes was then taken over by the IUPAC/IUB Commission on Biochemical Nomenclature (CBN). This Commission was originally set up to deal with the nomenclature of various compounds of biochemical interest. At a meeting in September, 1969, it was decided that the *Recommendations on Enzyme Nomenclature* should be revised, mainly to include the many enzymes discovered in recent years, and an Expert Committee on Enzymes was formed, consisting of A.E. Braunstein, J.S. Fruton, O. Hoffmann-Ostenhof, B.L. Horecker, W.B. Jakoby, P. Karlson, B. Keil, E.C. Slater, E.C. Webb *(convenor)* and W.J. Whelan. With the help of a number of expert subcommittees, and comments and suggestions solicited from authors and editors, a completely revised version of Enzyme Nomenclature was prepared and published as *Recommendations (1972) of the International Union of Pure and Applied Chemistry and the International Union of Biochemistry.*

After the publication of the third version of the complete report and enzyme list, the Commission on Biochemical Nomenclature decided that it would be appropriate to publish from time to time, a supplement to the Enzyme List, containing new entries, deletions and corrections. The first supplement was prepared during 1974-5 and published in Biochimica et Biophysica Acta (Vol. 429, pages 1-45 (1976).

During 1977 there was a reorganization of responsibility for consideration of biochemical nomenclature, and the responsibility for enzyme nomenclature passed to the new Nomenclature Committee of I.U.B.. At the same time the International Union of Biochemistry was able to arrange with the National Institutes of Health at Bethesda to enter the enzyme list on computer tape and prepare future versions of the list as a computer print-out. This phase of the operation was under the direction of Richard J. Feldmann of the Division of Computor Research and Technology, National Institutes of Health. The present version of Enzyme Nomenclature is the first to be produced in this way. It includes changes and additions approved by the Nomenclature Committee of I.U.B. at meetings in June 1977 and June 1978.

The number of enzymes in the various versions of the enzyme list are as follows:

Report of the Enzyme Commission (1961)	712
Enzyme Nomenclature (1964)	875
Enzyme Nomenclature (1972)	1770
Enzyme Nomenclature (1972)plus Supplement I (1975)	1974
Present version	2122

Many people have contributed to the steady growth of the Enzyme List. Particular mention should be made of Otto Hoffmann-Ostenhof, who was Secretary of the original Enzyme Commission, and as Chairman of the Commission on Biochemical Nomenclature from 1965 to 1976, has been largely responsible for continuity of the efforts in this field. Until 1976, Alexander E. Braunstein had a similarly long association with this work. Until the transfer of the enzyme list to the computer in 1977, it has been kept in the form of a card index in the office of Edwin Webb, first at the University of Queensland, and more recently at Macquarie University, Sydney. In both places, for a period of 15 years, Miriam Armstrong has been responsible for the management of the list and typed the many versions of Enzyme Nomenclature (1964) and its subsequent edition and supplement.

CHAPTER 2

THE CLASSIFICATION AND NOMENCLATURE OF ENZYMES

1. General principles

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

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 synthetase system.

In this context it is appropriate to express disapproval of a loose and misleading practice that is currently rather frequent in 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 recent 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 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 enzyme (whether it is a flavoprotein, a haemoprotein, a pyridoxal-phosphate-protein, a cuproprotein, 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 this revised report in certain cases where classification based on specificity is difficult, for example with the proteinases (sub-sub-groups 3.4.21-24). 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 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 phosphatase.

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.* L-malate glyoxylate-lyase (CoA-acetylating) (EC 4.1.3.2, *cf.* section 3).

For the classification 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.

2. Systematic and trivial 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 has been strongly criticised. It has been pointed out that in many cases the reaction catalysed, given in parentheses, 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 has discussed this problem at length. 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 *Recommended Name.* Also, in the index the recommended names appear in bold roman. Nevertheless, it was decided to retain the systematic names as the basis for classification as well as for identification (to be given only once in the paper) 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) recommended names for new enzymes are generally formed as a condensed version of the systematic name; therefore, the systematic names are helpful in finding recommended 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 recommended 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 recommended name may 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 IUB.

The enzyme list at the end of this volume, in contrast to the earlier versions, 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. In those cases where there is a major paper describing the purification and specificity of an enzyme, 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 of classification and numbering of enzymes

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 sub-class,

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

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

The sub-classes and sub-sub-classes are formed according to principles indicated below; the full key to the classification is given in section 5.

The main divisions and sub-classes are:

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 recommended 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 indicates the group in the hydrogen donor which undergoes oxidation: 1 denotes a -CHOH- group, 2 an aldehyde- or keto-group, and so on, as listed in section 5.

The third figure, except in sub-groups 1.11 and 1.15, indicates the type of acceptor involved: 1 denotes NAD(P), 2 a cytochrome, 3 molecular oxygen, 4 a disulphide, 5 a quinone or related compound, *etc.*.

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 sub-class 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. The stereospecificity of a large number of dehydrogenases has been summarized*

2. TRANSFERASES. Transferases are enzymes transferring a group, *e.g.* the 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 recommended 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 aminotransferases (see below).

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

$$X - Y + Z = X + Z - Y$$

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.*

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* You, K., Arnold, L.J., Jr., Allison, W.S. & Kaplan, N.O. *Trends Biochem. Sciences,* Vol. 3, December 1978; a fuller compilation is available as TIBS Databank No. 2.

Another problem is posed in the enzyme-catalysed transamination reactions. They involve the transfer of one electron pair and a proton, together with the NH_2 group, from a primary amine to an oxo compound, according to the general equation

$$R^1{-}CHNH_2{-}R^2 + R^3{-}CO{-}R^4 \xrightarrow{\text{enzyme}} R^1{-}CO{-}R^2 + R^3{-}CHNH_2{-}R^4.$$

The reaction can formally be considered 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 justifies allocation of these enzymes among the transferases as a special sub-group (2.6.1, aminotransferases).

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

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

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 recommended 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 among 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 are the so-called 'esterolytic' proteases, which hydrolyse ester bonds in appropriate substrates even more rapidly than natural peptide bonds. In this case, classification among the peptide hydrolases was 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: 3.1 are the esterases, 3.2 the glycosidases, and so on (*cf.* section 5).

The third figure normally specifies the nature of the substrate, *e.g* in the esterases the carboxylic ester hydrolases (3.1.1), thiol ester hydrolases (3.1.2), phosphoric monoesterases (3.1.3); in the glycosidases the *O*-glycosidases (3.2.1), *N*-glycosidases (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 (*cf.* section 5 for the full key).

4. LYASES. Lyases are enzymes cleaving **C-C, C-O, C-N,** and other bonds by elimination, leaving double bonds, 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 recommended names, expressions like *decarboxylase, aldolase, dehydratase* (in case of elimination of 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 sub-classes of the lyases include pyridoxal-phosphate enzymes that catalyse the elimination of β- or γ-substituent from an α-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 α,β(or β, γ)-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 β-synthase (EC 4.2.1.22).

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

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

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 *cyclo-isomerases.*

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

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

6. LIGASES (SYNTHETASES). Ligases are enzymes catalysing the joining together of two molecules coupled with the hydrolysis of a pyrophosphate bond in ATP or a similar triphosphate. The bonds formed are often *high energy* bonds. The systematic names are formed on the system *X:Y ligase (ADP-forming).* In the recommended nomenclature the term *synthetase* may be used, if no other short term (*e.g.* carboxylase) is available. Names of the type 'X-activating enzyme' should not be used.

The second figure in the code number indicates the bond formed: 6.1 for C-O bonds (enzymes acylating tRNA), 6.2 for C-S bonds (acyl-CoA derivatives) *etc.*. Sub-sub-classes are only in use in the C-N ligases (*cf.* section 5).

In a few cases it is necessary to use the word *other* in the description of sub-classes and sub-sub-classes. They have been provisionally given the figure 99, in order to leave space for new subdivisions. Actually, in the revised Enzyme List presented here, a number of new sub-classes and sub-sub-classes have been introduced.

Some enzymes have been deleted from the List, 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:

[n.m.o.p. *Deleted entry: old name]*

or

[n.m.o.p. *Transferred entry: now EC q.r.s.t. - recommended 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 will become necessary from time to time, and will have to be carried out by future enzyme commissions or Expert Committees of NC-IUB.

4. Rules for classification and nomenclature

(a) GENERAL RULES AND GUIDELINES

Guidelines for recommended names

1. Generally accepted trivial names of substrates may be used in enzyme names. The prefix D- should be omitted for common sugars and L- for individual amino acids, unless ambiguity would be caused. If desired, α,β,γ may be used instead of numbers to indicate positions where such usage is widely established at present; in general, it is not necessary to indicate positions of substituents in recommended names, unless it is necessary to prevent two different enzymes having the same name. The prefix *keto* is used in the non-systematic names for derivatives of sugars in which -CHOH- has been replaced by -CO-.

Rules for systematic nomenclature, on which the classification is based

1. 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 α,β,γ system; α,β should be used for indicating configuration, although group names such as β-aspartyl-, γ-glutamyl-, and also β-alanine, γ-lactone are permissible. For nucleotide radicals, *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.

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'.

Guidelines for recommended names

Rules for systematic nomenclature, on which the classification is based

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 be used instead of names of substrates. Abbreviations for names of enzymes, *e.g.* GDH, should not be used.

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 adjustives, *e.g.* glucose-6-phosphate dehydrogenase (EC 1.1.1.49*).

5. The use as enzyme names of *descriptions* such as *condensing enzyme, Zwischenferment, 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.

6. If it can be avoided, a recommended 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.

7. 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 recommended name is based on the same general principles as the systematic name (see opposite), but with a minimum of detail, to produce a name short enough for convenient use. A few names of proteolytic enyzmes ending in *-in* are retained; all other enzymes names should end in *-ase. [The termination -ese should not be used.]*

7. 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, with small and equal spaces before and after the colon. The second part, ending in *-ase*, indicates the nature of the reaction. 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).*

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

9. A number of additional generic words indicating reaction types are used in recommended names, but not in the systematic nomenclature, *e.g. dehydrogenase, reductase, oxidase, peroxidase, kinase, tautomerase, deaminase, dehydratase, etc..*

* This follows standard practice in phrases where two nouns qualify a third.