

# A Brief Guide to Enzyme Nomenclature and Classification

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## 1) Introduction

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NC-IUBMB Enzyme List, or, to give it its full title, “Recommendations of the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology on the Nomenclature and Classification of Enzymes by the Reactions they Catalyse,<sup>1</sup> is a functional system, based solely on the substrates transformed and products formed by an enzyme. The basic layout of the classification for each enzyme is described below with some indication of the guidelines followed. More detailed rules for enzyme nomenclature and classification are available online.<sup>2</sup> Further details of the principles governing the nomenclature of individual enzyme classes are given in the following sections.

## 2. Basic Concepts

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### 2.1. EC numbers

Enzymes are identified by EC (Enzyme Commission) numbers. These are also valuable for relating the information to other databases. They were divided into 6 major classes according to the type of reaction catalysed and a seventh, the translocases, was added in 2018.<sup>3</sup> These are shown in Table 1.

**Table 1. Enzyme classes**

	Name	Reaction catalysed
1	Oxidoreductases	*AH <sub>2</sub> + B = A + BH <sub>2</sub>
2	Transferases	AX + B = BX + A
3	Hydrolases	A-B + H <sub>2</sub> O = AH + BOH
4	Lyases	A=B + X-Y = A-B     X Y
5	Isomerases	A = B
6	Ligases	†A + B + NTP = A-B + NDP + P (or NMP + PP)
7	Translocases	AX + B    = A + X +    B (side 1)                    (side 2)

\*Where nicotinamide-adenine dinucleotides are the acceptors, NAD<sup>+</sup> and NADH + H<sup>+</sup> are used, by convention.

†NTP = nucleoside triphosphate.

The EC number is made up of four components separated by full stops. The first identifies the class of reaction catalysed. The second number (the subclass) generally contains information about the type of compound or group involved. For the oxidoreductases, the subclass indicates the type of group in the donor that undergoes oxidation or reduction (e.g., 1.1. acts on the CH-OH group of donors whereas 1.4. acts on the CH-NH<sub>2</sub> group of donors). New subclasses may be created as new information or interpretations become available, e.g., a new subclass, EC 5.6: ‘[Isomerases altering macromolecular conformation](#)’ has recently been added to the Isomerases class.

The third number, the sub-subclass, further specifies the type of reaction involved. For instance, EC 1.x.1.- indicates that NAD<sup>+</sup> or NADP<sup>+</sup> is the acceptor, while 1.x.2.- has a cytochrome as the acceptor, etc. The fourth is a serial number that is used to identify the individual enzyme within a sub-subclass. Fig. 2 illustrates the use of this system for the ligases with EC 6.3 expanded to show the complete sub-subclasses.

A list of the numbers for different enzyme classes etc. can be found online.<sup>4</sup>

**Fig. 2. Enzyme classes with EC 6.3 expanded**

[+subclass]. [+sub-subclass]. [+serial]

<b>EC 1</b>	[+]	<b>Oxidoreductases</b>
<b>EC 2</b>	[+]	<b>Transferases</b>
<b>EC 3</b>	[+]	<b>Hydrolases</b>
<b>EC 4</b>	[+]	<b>Lyases</b>
<b>EC 5</b>	[+]	<b>Isomerases</b>
<b>EC 6</b>	[-]	<b>Ligases</b>
EC 6.1	[+]	Forming carbon-oxygen bonds
EC 6.2	[+]	Forming carbon-sulfur bonds
EC 6.3	[-]	Forming carbon-nitrogen bonds
EC 6.3.1	[+]	Acid—ammonia (or amine) ligases (amide synthases)
EC 6.3.2	[+]	Acid—amino-acid ligases (peptide synthases)
EC 6.3.3	[+]	Cyclo-ligases
EC 6.3.4	[+]	Other carbon-nitrogen ligases
EC 6.3.5	[+]	Carbon-nitrogen ligases with glutamine as amido-N-donor
EC 6.4	[+]	Forming carbon-carbon bonds
EC 6.5	[+]	Forming phosphoric-ester bonds
EC 6.6	[+]	Forming nitrogen—metal bonds
<b>EC 7</b>	[+]	<b>Translocases</b>

## 2.2. Enzyme entries

In addition to the EC number, each enzyme is described by the fields described below. An illustrative example is shown in Fig. 2.

### Fig. 2. Example enzyme entry

# ExplorEnz - The Enzyme Database



Home	Search	Enzymes by Class	New/Amended Enzymes	Statistics	Forms	News	Information	Downloads
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Your query returned 1 entry. Printable version

## EC 1.1.1.282

Accepted name: quinate/shikimate dehydrogenase

Reaction: (1) L-quininate + NAD(P)<sup>+</sup> = 3-dehydroquininate + NAD(P)H + H<sup>+</sup>  
(2) shikimate + NAD(P)<sup>+</sup> = 3-dehydroshikimate + NAD(P)H + H<sup>+</sup>

For diagram of shikimate and chorismate biosynthesis, [click here](#)

Glossary: **quininate** = (1R,3R,4R,5R)-1,3,4,5-tetrahydroxycyclohexanecarboxylic acid and is a cyclitol carboxylate

The numbering system used for the 3-dehydroquininate is that of the recommendations on cyclitols, sections I-8 and I-9: and is shown in the [reaction diagram](#)). The use of the term '5-dehydroquininate' for this compound is based on an earlier system of numbering.

Other name(s): YdiB

Systematic name: L-quininate:NAD(P)<sup>+</sup> 3-oxidoreductase

Comments: This is the second shikimate dehydrogenase enzyme found in *Escherichia coli* and differs from EC 1.1.1.25, shikimate dehydrogenase, in that it can use both quinate and shikimate as substrate and either NAD<sup>+</sup> or NADP<sup>+</sup> as acceptor.

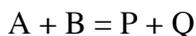
Links to other databases: [BRENDA](#), [EXPASY](#), [KEGG](#), [MetaCyc](#), [PDB](#)

- References: 1. Michel, G., Roszak, A.W., Sauvé, V., Maclean, J., Matte, A., Coggins, J.R., Cygler, M. and Laphom, A.J. Structures of shikimate dehydrogenase AroE and its paralog YdiB. A common structural framework for different activities. *J. Biol. Chem.* 278 (2003) 19463–19472. [DOI] [PMID: 12637497]
2. Benach, J., Lee, I., Edstrom, W., Kuzin, A.P., Chiang, Y., Acton, T.B., Montelione, G.T. and Hunt, J.F. The 2.3-Å crystal structure of the shikimate 5-dehydrogenase orthologue YdiB from *Escherichia coli* suggests a novel catalytic environment for an NAD-dependent dehydrogenase. *J. Biol. Chem.* 278 (2003) 19176–19182. [DOI] [PMID: 12624088]

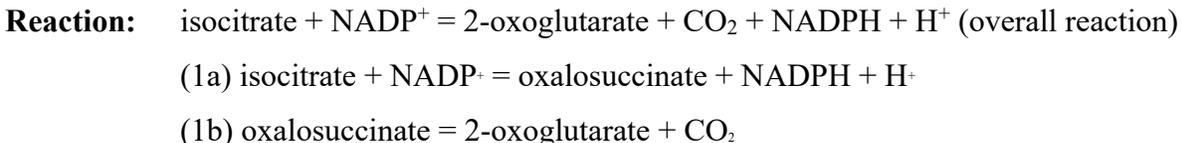
[EC 1.1.1.282 created 2004]

**Accepted name:** The most commonly used name for the enzyme, provided that it is neither unambiguous nor misleading. A number of generic words indicating reaction types may be used in accepted names, but not in the systematic names, e.g. *dehydrogenase*, *reductase*, *oxidase*, *peroxidase*, *kinase*, *tautomerase*, *deaminase*, *dehydratase*, *synthase*, etc. Where additional information is needed to make the reaction clear, a phrase indicating the reaction or a product may be added in parentheses after the second part of the name, e.g. (*ADP-forming*), (*dimerizing*), (*CoA-acylating*).

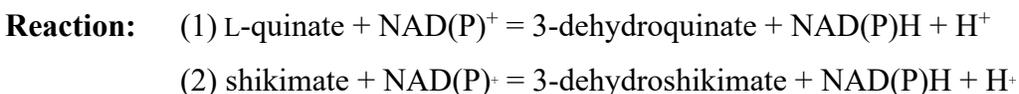
**Reaction:** The actual reaction catalysed, written, where possible, in the form of a 'biochemical' balancing equation of the type



This formulation gives no indication of the preferred equilibrium position of the reaction or, indeed, whether it is readily reversible. In the case of reversible reactions, the direction chosen for the reaction and systematic name is the same for all the enzymes in a given class, even if this direction has not been demonstrated for all. Frequently, such biochemical equations are not charge-balanced. Indeed, it would not be practicable to do so since the pH is not specified. Although the classification system is based on the overall reaction catalysed, some processes are known to involve two or more successive steps. This is dealt with by showing them below the overall reaction as illustrated for the reaction catalysed by isocitrate dehydrogenase (NADP<sup>+</sup>); EC 1.1.1.42:



Reactions and classification are based on substrates that are known to occur physiologically and “synthetic substrates” are not considered. However when an enzyme can act on more than one substrate with similar efficiency this may be indicated by showing more than one reaction, as illustrated for quinate/shikimate dehydrogenase (EC 1.1.1.182):



**Other name(s):** Any other names that have been used for the enzyme. This is to be as comprehensive a list as possible to aid searching for any specific enzyme. The inclusion of a name in this list does not mean that its use is encouraged. In some cases where the same name has been given to more than one enzyme, this ambiguity will be indicated. When gene names are also included these are indicated as such.

**Systematic name:** This attempts to describe in unambiguous terms what the enzyme actually catalyses. 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. A number of generic words indicating a type

of reaction may be used in either accepted or systematic names: *oxidoreductase*, *oxygenase*, *transferase* (with a prefix indicating the nature of the group transferred), *hydrolase*, *lyase*, *racemase*, *epimerase*, *isomerase*, *mutase*, *ligase*. 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, as in the case of the accepted names.

**Comments:** Brief comments on the nature of the reaction catalysed, possible relationships to other enzymes, species differences, metal-ion requirement, etc.

**References:** Key references on the identification, nature, properties and function of the enzyme. They are not intended to be comprehensive.

### 2.3. Other information

In addition to the above, the following may be included if thought desirable.

**Glossary:** The Glossary is used to relate the common names of the compounds shown in the reaction field or accepted names with their IUPAC names, and any alternative names that may be used. This can be accessed separately,<sup>5</sup> where the entries are each linked to the Royal Society of Chemistry ChemSpider database<sup>6</sup> to allow access to their structures and other chemical information. The NC-IUBMB works closely with the IUPAC on the Joint Committee on Biochemical Nomenclature to ensure that these names accord with the IUPAC system.<sup>7</sup> For commonly used biochemical abbreviations, a list of those used without definition is also provided.<sup>8</sup>

**Diagrams:** Many entries are linked to diagrams that show the involvement of the enzyme in a metabolic pathway and/or its reaction mechanism. These diagrams were developed by H. B. F. Dixon and G. P. Moss, and are now being maintained and expanded by G. P. Moss.

## 3. Access

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ExplorEnz<sup>1,9</sup> is the primary source for all enzymes classified by the IUBMB. It was developed in order to facilitate curation of the enzyme nomenclature data, to maintain correct data formatting, and to facilitate its use by other databases. Options for both simple substring searching and more complex searches were also provided. The data are freely available and are reproduced by many

other databases, as well as at the Queen Mary University of London Enzyme Nomenclature website.<sup>9</sup> Direct links to some sites that provide additional information are provided with enzyme entry. Associated, private, websites<sup>10</sup> have been developed that allow draft entries to be prepared with automated formatting of new and revised entries (including references), and a complete log of changes made, along with timestamping, etc.

#### **4. New Enzymes and amended entries**

The Enzyme list presently contains over 6000 entries and the number is steadily increasing as new ones are discovered and characterized. Proposals for new enzymes to be included are always welcome and forms for this are provided at the ExplorEnz website.<sup>10</sup> It should be noted that the functional criterion means that the reaction must have been characterized and that for a new enzyme to be included it must catalyse a reaction that is different from any that are already listed. Before a new enzyme is added to the official Enzyme List, is assessed by a group appointed by the IUBMB, which currently comprises Kristian Axelsen (Switzerland), Ron Caspi (USA), Masaaki Kotera (Japan), Andrew McDonald (Ireland), Gerry Moss (UK), Dietmar Schomburg, Ida Schomburg (Germany) and Keith Tipton (Ireland), who prepare the full entries. These then undergo a one-month public-review process,<sup>12</sup> during which time the entry may be modified or considered unsuitable for inclusion in the official list. Existing enzyme entries that have been modified substantially also go through this public-review process. Public feedback on these enzyme entries is particularly important to ensure that they are as correct as possible. While new enzymes are undergoing public review, the EC number should not be cited. In cases where newer information indicates that an entry should be deleted or transferred to a new class, the original EC number is not used again but retained with an indication to that effect.

#### References

1. <https://www.enzyme-database.org/>
2. <https://www.enzyme-database.org/rules.php>
3. Tipton, K. Translocases (EC 7): A new EC Class. *Enzyme Nomenclature News*, August 2018.
4. <https://www.enzyme-database.org/class.php>

5. <https://www.enzyme-database.org/glossary.php>
6. <http://www.chemspider.com/>
7. Panico R, Powell WH & Richer J-C (1994) A Guide to IUPAC Nomenclature of Organic Compounds. Blackwell Science, Oxford
8. <https://www.enzyme-database.org/abbrev.php>
9. <http://www.sbc.sqmul.ac.uk/iubmb/enzyme/>
10. McDonald AG, Boyce S & Tipton KF (2009) ExplorEnz: the primary source of the IUBMB enzyme list. Nucleic Acids Res 37, D593–D597.
11. <http://www.enzyme-database.org/forms.php>
12. <http://www.enzyme-database.org/newenz.php>

Table and Figures