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Hazard Classification of Enzymes Under the 2012 OSHA Hazard Communication Standard (29 C.F.R. § 1910.1200)¹

Classification of Enzyme Substances

Enzymes can be grouped into three hazard classes, based on enzyme type. The recommended hazard classification of enzymes in each class is outlined in the table below. The Enzyme Technical Association's (ETA) recommendations are based on the weight of evidence from the best available data.

Note: These classifications are likely to change over time as more test data becomes available.

Enzyme Class	Hazard Classification
Protease (Subtilisin)	Acute Toxicity (Oral) Category 4 Skin Irritant Category 2 Eye Irritant Category 2B Respiratory Sensitizer Category 1* Specific Target Organ Toxicant – Single Exposure (Respiratory Irritant) Category 3
Protease (Other)	Skin Irritant Category 2 Respiratory Sensitizer Category 1*
Non-protease	Respiratory Sensitizer Category 1*

* The ETA believes that available data is not sufficient for sub-categorization. Therefore, enzymes should be classified as Respiratory Sensitizer Category 1.

OSHA does not have the regulatory authority to require classification of environmental hazards. However, information on environmental hazards may be provided in Section 12 of the Safety Data Sheet, formerly known as the Material Data Safety Sheet (MSDS).

¹ The regulation, its appendices and its tables may be found at the Government Printing Office's ("GPO") website, available at <http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&rgn=div8&view=text&node=29:6.1.1.1.1.1.1.36&idno=29> (last visited Aug. 28, 2013).

Classification of mixtures

Hazard classification of enzyme mixtures should be performed according to the best available data. For hazard classification purposes, test data should be considered according to the hierarchy below:

1. Classification based on test data for the complete mixture
2. Classification based on test data for a similar mixture using bridging principles
3. Classification based on application of cut-off values/concentration limits for all components of the mixture as outlined in Appendix A to 29 C.F.R. § 1910.1200.

The generic cut-off concentrations relevant to enzyme mixture classification under the U.S. Hazard Communication Standard are summarized in the table below.

Hazard Category	Cut-off Concentration Triggering Classification of An Enzyme* Mixture
Acute Toxicity (Oral) Category 4	≥ 90% (TABLE A.1.1)
Skin Irritant Category 2	≥ 10% (TABLE A.2.3)
Eye Irritant Category 2B	≥ 10% (TABLE A.3.3)
Respiratory Sensitizer Category 1	≥ 0.1% (TABLE A.4.5)
Specific Target Organ Toxicant – Single Exposure Category 3	≥ 20% (TABLE A.8.3.4.5)

*Active enzyme protein, calculated on the basis of the declared enzyme activity

The presence of other hazardous components in the mixture may require classification below the generic cut-off concentrations. Some hazard classifications are additive (e.g., skin and eye irritation) and would require consideration of the sum concentration in the mixture. In general, enzyme concentrations should not be considered additive when classifying mixtures for respiratory sensitization. Only if there is evidence of immunological cross-reactivity should enzyme concentrations be cumulative for respiratory sensitization classification.

Obligation to Classify Based on Available Data

All manufacturers and importers are required to evaluate the intrinsic hazardous properties of their materials. Manufacturers and importers must then classify and communicate the hazards according to the requirements of the U.S. Hazard Communication Standard (29 C.F.R. § 1910.1200). Employers are also required to evaluate and communicate the hazards associated with materials in the workplace. Manufacturers, importers, and employers are obligated to consider the total weight of evidence. All available relevant information must be

considered, including the results of valid in vitro tests, relevant animal data, and human experience, such as epidemiological and clinical studies and well-documented case reports and observations.

Label Content

Required label elements are outlined in Appendix C to 29 C.F.R. § 1910.1200. Labels on hazardous materials must include:

- The product identifier (consistent with the identifier used on the safety data sheet)
- The name, address, and telephone number of the manufacturer, importer, or responsible party (on shipped containers)
- A signal word
- All applicable hazard pictograms
- All applicable hazard statements
- Precautionary statements

Enzyme manufacturers and importers should take note of section C.2.1.4 of 29 C.F.R. § 1910.1200, which states that “[i]f the health hazard pictogram is included for respiratory sensitization, the exclamation mark pictogram shall not appear where it is used for skin sensitization or for skin or eye irritation.” Thus, the exclamation mark pictogram should not be included on protease labels even if the material is classified as irritating to eyes and/or skin.

Label Size

Unlike other regions, the United States does not specify minimum size requirements for hazard labels. The labels should be large enough to effectively communicate the required information.

Label Color

A pictogram must be provided in the standard diamond shape. The pictogram must be black on a white background. The frame around the pictogram must be red. An empty red frame without a hazard symbol is not permitted on the label.

Statement Selection

The text of all applicable hazard statements is required on the label. The phrase code (e.g. H334) is not required. The text of applicable precautionary statements is required on the label. Precautionary statements may be combined to improve readability. If classification results in similar precautionary statements, the most stringent statement can only be applied to eliminate redundancy. There is no required precedence of precautionary statements, but the ordering of statements on the label can be adjusted when appropriate. See the examples below:

Example 1: Combining statements

“Keep away from heat, sparks and open flame,” “Store in a well-ventilated place” and “Keep cool” can be combined to read “Keep away from heat, sparks and open flame and store in a cool, well-ventilated place.”

Example 2: Giving statement precedence

If a chemical is carcinogenic and acutely toxic, rapid action may be crucial following acute exposure. First aid measures for acute toxicity may take precedence on the label over those for long-term effects.

Labeling of Unknown Toxicity

OSHA requires special labeling of mixtures containing substances with unknown acute toxicity. When an ingredient with unknown acute toxicity is used in a mixture at a concentration of $\geq 1\%$, a statement that “X% of the mixture consists of ingredient(s) of unknown acute toxicity” is required on the label. This requirement can be avoided by testing the acute toxicity of the mixture.