<u>Guide to the Safe Handling of</u> <u>Enzyme</u>

Amano Enzyme Inc.

Version 1

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1. What Are Enzymes?

Enzymes are proteins produced in living cells of plants, animals, and microorganisms and catalyzing biological reactions essential for life support. Enzymes manufactured under advanced manufacturing and quality control systems are utilized in the fields of pharmaceuticals, food, feed, industry, and clinical diagnosis to accelerate the synthesis, degradation, and oxidation/reduction of organic substances such as carbohydrates, fats, and proteins.

2. Enzyme Properties

1) Usefulness of enzymes

Enzymes have excellent properties of exclusively acting on specific substances (substrate specificity) under mild conditions (ambient temperature, ambient pressure, approximately neutral pH). For example, digestive enzymes break down food into nutrients. Starch saccharifying enzymes (for glucose production) break starch into glucose. These properties are applied to a wide range of applications, and many enzymes are used in various places in life. The use of enzymes for food industry is presented below.

[Protein processing]

Proteases (proteolytic enzymes) are mainly used to improve the taste, yield of extracts, nutritional value, and physical properties through degradation of proteins.

[Starch processing]

A variety of sugars with useful properties (glucose, maltose, maltotriose, branched oligosaccharide, cyclodextrin, isomerized sugar, and fructose) are produced using various enzymes that act on glycosidic bonds in starch.

[Yeast extract]

Yeast extract is obtained from yeast such as brewer's yeast, baker's yeast, and torula yeast by extraction involving self-digestion or enzymatic degradation and concentration. It is widely used as an umami seasoning that contains amino acids, inosinic acid, guanylate, etc.

[Fat processing]

Lipases are used in the field of fat and processing in food industry. Lipases (fat-degrading enzymes) are enzymes mainly hydrolyzing triglycerides to produce fatty acids and glycerin. Applications include production of milk flavors, improvement of triglyceride purity, and concentration of highly unsaturated fatty acids (EPA, DHA).

[Miscellaneous]

For other uses, refer to the product uses on our website.

3. Health Effects

Enzymes may sometimes cause irritation of the skin (skin irritation). In susceptible individuals, Inhalation of enzymes may elicit an immune response (sensitization). Exposures repeated over time may induce production of allergic antibodies and further exacerbation of symptoms may lead to development of respiratory allergy. Therefore, when working with enzymes, care should be taken to avoid inhalation of fine powders and aerosols as well as their contact with skin, eyes, etc. On the other hand, in handling enzymes, proper working practices, process control and use of appropriate personal protective equipment can minimize adverse health effects and secure safety in work. Specific allergic symptoms and irritation during enzyme exposure are detailed below as basic information required for appropriate management.

4. Symptoms Developing on Enzyme Exposure

1) Allergy

As with protein allergens such as pollen, enzymes may cause mild to severe symptoms such as sneezing, nasal obstruction and sinus congestion, cough, watery eyes and runny nose. With the onset and progression of occupational asthma, more serious symptoms may occur such as tightness of the chest, wheezing and shortness of breath. These symptoms may develop during work hours or even two or more hours after work exposure. Symptoms occur in allergic patients inhaling enzyme aerosols and usually disappear within a few hours. Common seasonal allergy symptoms may resemble enzyme allergies. If symptoms appear more often on working days and disappear during weekends or holidays, they may be due to enzyme exposure and should be investigated. People with allergic symptoms should immediately report their symptoms and ask a physician for a diagnosis.

2) Irritation

While the primary health hazard associated with enzymes is respiratory allergy, contact with proteolytic enzymes may cause skin and eye irritation. The higher the concentration of the enzyme preparation, the greater the potential for producing irritation upon contact. This irritation is caused by catalytic activities of proteolytic enzymes and is not an allergic response.

Non-proteolytic enzymes have not been shown to cause skin and eye irritation. However, as part of personal hygiene practices, skin and eye contact with all enzymes should be minimized. Please refer to the Safety Data Sheet (SDS) for information on the hazards associated with other ingredients of the enzyme preparation.

5. Handling of Enzymes

1) Measures for prevention of exposure

Exposure control

The risk associated with enzyme exposure can be controlled using a widely accepted hierarchy of controls including engineering controls, safe working practices, and personal protective equipment. Implementation of these controls depends on the likelihood and severity of enzyme exposure potentially associated with the work task.

Implementing engineering controls such as isolation or containment is the best method to minimize exposure. Isolation techniques are used to completely segregate the enzyme product from the employee and workplace by creating a barrier (e.g., closed dosing systems, direct tote connections). Although isolation is not feasible for some operations, exposure to hazards in such cases may be prevented by installing local exhaust ventilation (LEV) to accommodate enzyme products (in the packaging and rework area). It is important that all engineering

controls be properly maintained and tested for efficacy through routine enzyme monitoring and maintenance procedures.

Safe work - Prevention of and protection from enzyme dust (airborne microparticles)/aerosols Safe handling of enzyme preparations can be accomplished through working practices in conjunction with engineering controls and use of protective equipment. It is also important that workers are trained on the health hazards of enzymes, understand the symptoms of enzyme allergy and follow safe working practices that minimize the risk of exposure. In working with enzyme preparations, working practices should not generate aerosols or result in direct skin contact. Aerosols are formed through high-energy operations such as mixing, grinding, and some material transfers. Cleaning actions such as sweeping, blowing, steam cleaning, and high-pressure spraying will also generate aerosols and should be avoided.

The following safety measures are recommended to minimize exposure.

- Avoid inhalation of dust, droplets and mists.
- Wash hands with water and mild soap after contact with enzyme materials.
- Change the work clothes every day. Make sure to replace the work clothes every time when contaminated with enzyme raw materials.
- Prevent contact of the face or eyes with the work clothes or gloves contaminated with enzymes.
- 2) Protective equipment for work

Risk assessment/risk avoidance for workers (precautions for use)

Respiratory protective equipment

The use of respiratory protective equipment should be considered if engineering controls are not sufficient to control enzyme levels below recommended exposure limits. Personal protective equipment may be used as an auxiliary means when a specific task could result in high potential risk of exposure.

When using respiratory protective equipment, the filters should be N100/P100/P3, etc. These filters provide the appropriate level of protection to the user.



3) Protective clothing

Protective clothing should be worn when there is a potential for skin or eye contact. Protective clothing may include gloves and safety goggles as well as outer garments such as coveralls and lab coats. Protective clothing is particularly important when working with proteolytic enzymes known to cause skin irritation. Protective clothing should be removed prior to leaving the work area and must not be worn into other areas of the facility (e.g. lunchroom or offices). For all types of enzymes, protective clothing should be defined based on workplace activities and potential for exposures to avoid unintentional inhalation of any residual enzyme.

6. Measurement of Enzyme Dust in the Work Environment

Air monitoring techniques are available for measurement of enzyme dust or mist concentrations in the air to assess the effectiveness of engineering controls and the potential for exposure of employees. The American Conference of Governmental Industrial Hygienists (ACGIH) has established a threshold limit value (TLV) for only one class of enzyme, subtilisin, of 60 ng/m3 as a ceiling limit. This exposure limit should be recognized and employed for all enzyme classes. Please contact us for additional information.

7. Cleaning at the Time of Spillage / Cleaning and Maintenance of the Work Area

Whenever maintenance is to be performed on equipment that has been in contact with enzymes, the equipment should always be cleaned before starting the maintenance work. Personal protective equipment (gloves, protective masks, eye protection) should be used during maintenance operations where there is a potential for exposure or exposure potential is unknown.

8. First-aid Treatment in Case of Exposure

Skin contact

Flush the exposed skin thoroughly with water for 15 minutes, then wash with mild soap and water. Remove and clean any contaminated work clothing. Ensure that the handling of contaminated clothing does not expose another person.

Inhalation

Remove the individual from the exposure source to a well-ventilated area. Monitor them for irritation or allergic symptoms. If any symptoms appear, consult a physician. Symptoms may be delayed after exposure.

Eye contact

Rinse the eyes thoroughly with water for 15 minutes or more and then consult a physician.

9. Medical Surveillance (Regular Health Checkup)

Health management of workers handling enzymes shall be performed on the occasion of regular health checkups, etc. provided by each business operator. If any abnormality occurs during handling of enzymes, immediately seek diagnosis and consultation from the industrial physician appointed by each employer.

10. Training

All employees and contractors working with enzyme preparations should be properly trained in safe use and handling procedures as well as emergency measures such as spill cleanup and equipment maintenance. Such training is particularly necessary when the employee is new to the job or a new task is introduced. Many countries adopt the United Nations (UN) Globally Harmonized System (GHS) as the standard for hazard communication. While several different versions of the GHS standard are adopted globally, the pictograms and phrases used are the same. Enzymes are classified as "Respiratory Sensitizers." The symbol indicated in the pictogram below is referred to as the "Health Hazard" and used to denote Respiratory Sensitizers. It is necessary to ensure that workers are trained on how to read SDS documents and distinguish GHS classifications/pictograms.



