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AMFEP AND ETA GUIDELINE ON CONSUMER RISK ASSESSMENTS FOR ENZYME-CONTAINING PERSONAL CARE PRODUCTS AND COSMETICS

PURPOSE:

The purpose of this AMFEP/ETA position guideline is to inform both potential producers and users of enzymes in personal care products and cosmetics of the potential health risks of enzymes and to recommend the framework for conducting risk assessments to help ensure the safety of new enzyme-containing products.

Experience in the cleaning products industry demonstrates that the potential risk of adverse effects can be successfully managed by identifying the hazards, carefully assessing potential exposures, characterizing the risk, and then applying appropriate risk management (ACI, American Cleaning Institute, 2019). If the risks are not managed appropriately, the consequences may spread beyond a single product or company. This could lead to unwarranted limitations on the use of enzyme technology in other consumer applications. Good stewardship of enzymes involves accurate hazard characterization of enzyme-containing products and proper risk assessment for both existing and new uses to prevent the development of allergy in workers and consumers.

THE CONSUMER RISK ASSESSMENT PROCESS:

This process is divided into four steps, namely, hazard identification, dose-response assessment, exposure assessment and risk characterization. The risk assessment process for enzymes follows this general approach, but benchmark exposures to define effect and no-effect thresholds are used instead of classic dose-response curves. Benchmark values are based on studies in which measured or estimated exposure levels are associated with a demonstrated effect or the lack of a biological effect in the people exposed.

Hazard identification: The health hazards of commercially available enzymes have been well characterized through toxicological, epidemiological, and case studies (ACI, 2019). The toxicology of enzymes are generally unremarkable; acute, sub-acute, chronic, genotoxicity is not of concern for enzymes (Basketter et al 2012).

The main safety concern with enzymes is the potential induction of respiratory allergies, (Type 1 hypersensitivity) similar to allergic reactions to other protein allergens from pets, dust mites, pollens, etc. The symptoms can occur immediately or up to several hours after exposure to the allergen. In addition, some enzymes (proteases) in high concentrations may produce skin or eye irritation. Skin sensitization (Type IV delayed hypersensitivity) is not considered to be associated with enzyme products. This is supported by predictive testing in people (Basketter & Kimber 2022).

The dose-response assessment consists of determining the amount of exposure to relevant tissues (i.e., the delivered dose) and the corresponding biological effect. The delivered dose

will be a function of the level, duration, pattern, and route of exposure. This process is not trivial since the dose-response relationship for enzymes is not clearly defined for inhalation allergy. There remain limitations in our knowledge on safe levels of exposure and for example, the role of peak exposures in the development of enzyme-specific antibodies and elicitation of symptoms (ACI, 2019). Therefore, benchmark values rather than more traditional dose-response measures are generally used to support decisions in enzyme risk assessments. Such benchmark values are based on studies in which measured or estimated exposure levels are associated with a demonstrated effect or the lack of an effect in the people exposed.

Exposure assessment establishes the amount of enzyme the user may be exposed to during intended use, foreseeable misuse, and accidents. This value is then compared to the benchmark exposure to make risk decisions. When conducting an exposure assessment, several factors can influence exposure which need to be taken into consideration such as formulation and product type, delivery system, route of exposure, habits and practices (frequency of use, duration of use, amount of product per application and demographics of use/misuse) and accidental exposure. As a first step, a conservative theoretical calculation can be made. If this indicates that there is a potential for health effects in comparison to benchmark values, then measurements are carried out. Spray products have a higher potential for inhalation during use and therefore a quantitative risk assessment should be performed to assess potential exposures.

Benchmark values are based on studies in which measured or estimated exposure levels to enzymes are associated with a demonstrated effect or the lack of an effect in the people exposed. The effect can be the development of enzyme specific IgE antibody and/or the manifestation of allergic symptoms. For detergent enzymes, benchmark data have been generated from clinical studies, case studies and prospective monitoring of occupationally exposed populations. In general, one should be aware that the exposure data should be relevant to that particular use/misuse, and that the extrapolation from one product type to another may not be appropriate. There are several published reports on personal care products containing proteins that indicated respiratory sensitization from exposure. These include soap bar (Kelling et al, 1998), body lotion (Sarlo et al. 2004), and wheat protein (Yagami et. al, 2017). In general, benchmark data is not readily available for personal care products, and it is advised to generate data through a clinical study.

A more detailed description of benchmark studies can be found in the ACI document “Risk Assessment Guidance for Enzyme-Containing Products” (ACI, 2019), and the HERA (Human and Environmental Risk Assessment) projects “Risk assessment on Subtilisins (Protease)” and “Risk assessment on α-Amylases, Cellulases and Lipases” (HERA, 2005).

Risk characterization is the examination of the relationship between human exposure (calculated or measured) and the inherent toxicity of a substance to assess the likely incidence and severity of any effect. This step is important because it integrates information regarding the hazard identification and exposure assessment associated with use and foreseeable misuse of a product. Decisions taken during risk characterization become part of the risk management process.

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The objectives of the risk management process are to determine the significance of risks to human health, to ensure that the product use is and remains within the acceptable risk, and to effectively communicate risks, or lack thereof, to appropriate audiences.

AMFEP/ETA encourages that the appropriate risk assessment process be conducted prior to the introduction of enzymes in personal care and cosmetic products.

More detailed information on this topic can be found in the ACI guidance document entitled "Risk Assessment Guidance for Enzyme-Containing Products" (ACI, 2019).

References

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