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Skin sensitisation classification: Not appliable for industrial enzymes

AMFEP, the Association of Manufacturers and Formulators of Enzymes products, reiterates the reasons why a classification for skin sensitisation is not appliable for industrial enzymes, in accordance with the European CLP Regulation (1).

The ability of certain low molecular weight chemicals to induce skin sensitisation in humans, and upon further exposure to elicit the skin disease allergic contact dermatitis (ACD), has been known for over a century. Predictive models for skin sensitisation have been developed aiming at identifying those chemicals, which, due to their intrinsic properties, can modify skin protein and thereby induce contact allergy. Such chemicals are known as skin sensitisers and the consequence of exposure is referred to as skin sensitisation (2).
This hazard endpoint is part of the standard information requirements for any substance registered under the European REACH Regulation (Annex VII) (3), and also needs to be assessed for hazard communication according to the European CLP Regulation (1).

Article 5(1) of the European CLP Regulation provides the legal basis to evaluate if the hazard endpoint for skin sensitisation is applicable for industrial enzymes. The relevant available information for the purposes of determining whether the substance entails a physical, health or environmental hazard can be grouped into:

a) Test methods defined in the European REACH Regulation (3), or other sound scientific principles that are internationally recognised and validated according to international procedures;
b) Epidemiological data and experience on the effects on humans;
c) Any other new scientific information or information generated under internationally recognised chemical programmes.

Test methods

Enzymes are proteins and therefore the key aspects for skin sensitisation that need to be considered for proteins are also valid for enzymes. To date, no predictive model for assessing a skin sensitising potential of proteins is available that is internationally recognized and validated to international procedures. Thus, in the case of protein and enzyme allergenic potential, the use of present skin sensitisation models developed for low molecular chemicals, such as the murine local lymph node assay (LLNA), are inappropriate and misleading (2).

Epidemiological data

Industrial enzymes have been introduced into the European market 50 years ago. They are used in many industrial applications and are also an essential ingredient in some wide-spread uses, such as detergents. In these 50 years of use, the number of reported ACD cases in occupational health surveillance programmes and epidemiological studies following consumers using enzyme containing products (including soaps) is typically zero, or limited to isolated individuals and often correlating with a compromised skin barrier. Additionally, failure of enzymes to cause skin sensitisation is indicated by clinical studies, including human repeated insult patch tests (HRIPT) that yielded negative results (2,4).

Any other scientific information

A recent critical review carried out by Basketter and Kimber (2022) did not locate any other new relevant information on the potential of industrial enzymes causing skin sensitisation (4).

To conclude, and in accordance with the European CLP Regulation (1), the relevant available information do not support the classification of industrial enzymes as skin sensitisers.

References:

(1) Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures

(2) David A. Basketter, Ian Kimber, “Are skin sensitisation test methods relevant for proteins?”; Regulatory Toxicology and Pharmacology 99 (2018) 244–248

(3) Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

(4) David A. Basketter, Ian Kimber, “Enzymes and sensitisation via skin exposure: A critical analysis”; Regulatory Toxicology and Pharmacology 129 (2022) 105112