Accepted Manuscript

Industrial microbial enzyme safety: What does the weight-of-evidence indicate?

Gregory S. Ladics, Vincent Sewalt

PII: S0273-2300(18)30200-9

DOI: 10.1016/j.yrtph.2018.07.016

Reference: YRTPH 4179

To appear in: *Regulatory Toxicology and Pharmacology*

Received Date: 14 May 2018

Revised Date: 20 July 2018

Accepted Date: 22 July 2018

Please cite this article as: Ladics, G.S., Sewalt, V., Industrial microbial enzyme safety: What does the weight-of-evidence indicate?, *Regulatory Toxicology and Pharmacology* (2018), doi: 10.1016/j.yrtph.2018.07.016.

Industrial Microbial Enzyme Safety: What does the Weight-of-Evidence Indicate?

Gregory S. Ladics*[#], Ph.D., DABT, Fellow ATS and Vincent Sewalt^, Ph.D.

*DuPont Industrial Biosciences, Wilmington, DE USA

[#]Corresponding author: gregory.s.ladics@dupont.com; 302-695-6792

^DuPont Industrial Biosciences, Palo Alto, CA USA

Abstract

With the exception for the potential skin and eye irritating effects of some proteases, and the well-documented potential for respiratory sensitization in case of work place exposure, enzymes in general don't produce acute toxicity, dermal sensitization; genotoxicity, or repeated dose oral toxicity. Acute inhalation, reproduction, chronic toxicity, and carcinogenicity are not relevant for enzymes. Several hundred mutagenicity studies have been conducted on bacterial and mammalian cells using a variety of enzymes. No positive findings were observed. > 225 90-day studies have been performed and submitted to EFSA with no adverse findings, including in the bone marrow. The data showing no adverse effects for enzyme preparations also confirms that microbial metabolites and fermentation materials lack toxicity as well. Exposure to enzyme products is also minimal as recommended use levels are low, generally < 0.1% (wt/wt). The weight-of-evidence indicates that there are no concerns for oral toxicity of enzymes in general,