



EXECUTIVE SUMMARY:

DuPont Industrial Biosciences (IB) is seeking approval for a “Lipase, triacylglycerol (EC 3.1.1.3)” enzyme for production of bakery products such as, but not limited to, bread, Chinese stem buns, biscuits, steamed bread, cakes, noodles, pancakes, pasta, tortillas, wafers, and waffles. Lipase 3 will also be used for the production of beer and other cereal-based beverages. The enzyme is designated as “Lipase 3” throughout the dossier.

The enzyme Lipase 3 is derived from a selected non-pathogenic, non-toxigenic strain of *Trichoderma reesei* which is genetically modified to overexpress the Lipase 3 gene from *Aspergillus niger var. tubingensis* (hereafter referred to as *Aspergillus tubingensis*).

The enzyme is intended for use in the baking and brewing processes. In baking, Lipase 3 performs its technological function during the dough or batter handling to improve the dough stability and dough handling properties. In brewing processes, Lipase 3 performs its technological function in the mashing and fermentation step for removal of the fatty lipids which otherwise affect the mash separation and the yeast fermentation.

In all of these applications, Lipase 3 will be used as a processing aid where the enzyme is either not present in the final food or present in insignificant quantities having no function or technical effect in the final food.

To assess the safety of the Lipase 3 for use in these applications, Dupont IB vigorously applied the criteria identified in the guidelines as laid down by Food Standards Australia New Zealand (FSANZ) and U.S. Food and Drug Administration (FDA) utilizing enzyme toxicology/safety data, the safe history of use of enzyme preparations from *T. reesei* and of other lipase enzymes in food, the history of safe use of the *T. reesei* production organism for the production of enzymes used in food, an allergenicity evaluation, and a comprehensive survey of the scientific literature.

In addition, different endpoints of toxicity were investigated at MB Research Laboratories (Pennsylvania) and Harlan Laboratories (Switzerland) and the results are evaluated and assessed in this document. Lipase 3 is non-hazardous based on acute oral studies. In genotoxicity studies, Lipase 3 is not mutagenic, clastogenic or aneugenic. Daily oral administration of Lipase 3 up to and including a dose level of 160.6 mg total protein/kg bw/day or 123.15 mg TOS/kg bw/day does not result in any manifestation of systemic, hematologic, or histopathologic adverse effects.

Based on a worst-case scenario that a person is consuming Lipase 3 from the bakery products and brewing process, the calculated Theoretical Maximum Daily Intake (TMDI) will be 0.410 mg TOS/kg body weight/day. This still offers a 300× fold margin of safety.

Based on the results of safety studies and other evidence, Lipase 3 has been demonstrated as safe for its intended applications and at the proposed usage levels. Approval of this application would provide manufacturers and/or consumers with benefits of facilitating the baking or brewing process, lowering the manufacturing cost, and improving quality of final foods.