U. S. Food and Drug Administration
Center for Food Safety & Applied Nutrition
Office of Premarket Approval

Agency Response Letter
GRAS Notice No. GRN 000043

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Washington, DC 20204

September 22, 2000

Ms. Lori Gregg
Novo Nordisk BioChem North America, Inc.
77 Perry Chapel Church Road
Box 576
Franklinton, NC 27525

Re: GRAS Notice No. GRN 000043

Dear Ms. Gregg:

The Food and Drug Administration (FDA) is responding to the notice, dated April 25, 2000, that you submitted in accordance with the agency's proposed regulation, proposed 21 CFR 170.36 (62 FR 18938; April 17, 1997; Substances Generally Recognized as Safe (GRAS)). FDA received your notice on April 28, 2000 and designated it as GRN No. 000043.

The subject of your notice is lipase enzyme preparation derived from *Aspergillus oryzae* carrying a gene encoding lipase from *Thermomyces lanuginosus*. The notice informs FDA of the view of Novo Nordisk that this lipase enzyme preparation is GRAS, through scientific procedures, for use in dough, baked goods, and the fats and oil industry at minimum levels necessary to achieve the desired effect. The lipase enzyme preparation would be used as a catalyst in the interesterification of glycerides and acidolysis between glycerides and fatty acids in fats and oils at a maximum level of one kilogram of lipase per ton of triglycerides. The lipase enzyme preparation would be used in the hydrolysis of primary ester bonds in triglycerides in dough and baked goods for the purpose of modifying lipid-gluten interactions at a maximum level of one to five grams per 100 kg of flour.

In your notice, you describe: (1) a published review article about the safety of the host microorganism, *A. oryzae;* (2) scientific publications and recommendations issued by international organizations on the safety of enzymes used in food processing, including enzymes derived from genetically modified microorganisms; (3) published scientific articles that discuss the safety of the various components of the production organism, including the host organism, and the components of the genetic material that is

introduced into the host organism; (4) the basis for your conclusion that the presence of a gene encoding resistance to the antibiotic ampicillin is not a concern; (5) chapters in several books that discuss the manufacturing process, which includes standard methods for the fermentation, processing, and formulation of the enzyme preparation; and (6) a published review of oral toxicity and genetic toxicity studies conducted with the subject lipase enzyme preparation.

According to your notice, the enzyme preparation meets the specifications for enzyme preparations provided in the Food Chemicals Codex (4th ed., 1996). The enzyme preparation also meets the specifications for enzyme preparations provided by the Joint Expert Committee on Food Additives (JECFA; a joint committee of the Food and Agriculture Organization/World Health Organization).

Based on the information provided by Novo Nordisk, as well as other information available to FDA, the agency has no questions at this time regarding Novo Nordisk's conclusion that lipase enzyme preparation derived from a genetically modified strain of *A. oryzae* that contains a recombinant gene encoding *T. lanuginosus* lipase is GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding the GRAS status of the subject use of this enzyme preparation. As always, it is your continuing responsibility to ensure that food ingredients that you market are safe, and are otherwise in compliance with all applicable legal and regulatory requirements.

In accordance with proposed 21 CFR 170.36(f), a copy of the text of this letter, as well as a copy of the information in your notice that conforms to the information in proposed 21 CFR 170.36(c)(1), is available for public review and copying on the Office of Premarket Approval's homepage on the Internet (at http://vm.cfsan.fda.gov/~lrd/foodadd.html).

Sincerely,
/s/
Alan M. Rulis, Ph.D.
Director
Office of Premarket Approval
Center for Food Safety and Applied Nutrition

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