



James T. Heimbach, Ph.D., F.A.C.N.  
JHeimbach LLC  
4530 Broad Branch Road, N.W.  
Washington, DC 20008

Re: GRAS Notice No. GRN 000164

Dear Dr. Heimbach:

The Food and Drug Administration (FDA) is responding to the notice, dated March 2, 2005, that you submitted on behalf of Laboratorios Miret, S.A. (LAMIRSA) 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); the GRAS proposal). FDA received the notice on March 4, 2005, filed it on March 8, 2005, and designated it as GRAS Notice No. GRN 000164.

The subject of the notice is lauramide arginine ethyl ester (LAE). The major component of LAE is ethyl-N-alpha-lauroyl-L-arginate hydrochloride, which comprises 71 to 81 percent of non-dehydrated lauric arginate and 89 to 95 percent of the dehydrated form. The notice informs FDA of the view of LAMIRSA that LAE is GRAS, through scientific procedures, for use as an antimicrobial in certain foods including meat and poultry products at levels up to 200 parts per million (ppm)<sup>1</sup> of ethyl-N-Alpha-lauroyl-L-arginate hydrochloride.

As part of its notice, LAMIRSA includes the report of a panel of individuals (LAMIRSA's GRAS panel) who evaluated the data and information that are the basis for LAMIRSA's GRAS determination. LAMIRSA considers the members of its GRAS panel to be qualified by scientific training and experience to evaluate the safety of substances added to food. According to LAMIRSA's GRAS panel, ingestion of LAE from the intended uses results in a daily intake within safe limits established by published *in vitro* and *in vivo* studies and corroborated by unpublished animal and human studies.

LAMIRSA described the identity, composition and manufacture of LAE. LAMIRSA also provided product specifications for LAE.

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<sup>1</sup>Based on LAMIRSA's product specifications, 200 ppm of ethyl-N-alpha-lauroyl-L-arginate hydrochloride is equivalent to approximately 225 ppm dehydrated or 265 ppm non-dehydrated LAE.

In GRN 000164, LAMIRSA described a formulation, referred to as Mirenat-N, composed of LAE dissolved at specified concentrations in propylene glycol. FDA notes that propylene glycol is listed as a prohibited substance for use in or on cat food in 21 CFR 589.1001 and in the past, the Center for Veterinary Medicine has raised some concern regarding the use of propylene glycol in antimicrobials used for meat and poultry that could potentially be used in or on cat food.

LAMIRSA provides an estimated daily intake (EDI) of LAE. The EDI was calculated using LAMIRSA's use level and intended food categories as stated in GRN 000164 and food consumption data from the U.S. Department of Agriculture's 1994-96 Continuing Survey of Food Intakes by Individuals (CSFII) and its Supplemental Children's Survey (CSFII 1998). LAMIRSA reports that the mean 2-day average EDI of LAE by the population two years of age and older (eaters only) in the U.S. is 2.5 milligrams per kilogram body weight per day (mg/kg bw/day) and the 90<sup>th</sup> percentile EDI is 4.7 mg/kg bw/day. The mean and 90<sup>th</sup> percentile EDI of ethyl-N-alpha-lauroyl-L-arginate hydrochloride is 2.2 mg/kg bw/day and 4.2 mg/kg bw/day, respectively.

LAMIRSA discusses published and unpublished acute and subchronic animal studies, and describes generally available information about the absorption, distribution, metabolism, and elimination of LAE. LAMIRSA concludes that all of these studies indicate that long-term consumption of LAE is well-tolerated.

#### **Use in Meat and Poultry Products**

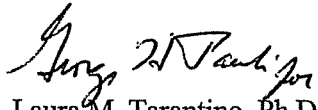
During its evaluation of GRN 000164, FDA consulted with the Labeling and Consumer Protection Staff of the Food Safety and Inspection Service (FSIS) of the United States Department of Agriculture (USDA). Under the Federal Meat Inspection Act and the Poultry Products Inspection Act, FSIS is responsible for determining the efficacy and suitability of food ingredients in meat and poultry products as well as prescribing safe conditions of use. Suitability relates to the effectiveness of the ingredient in performing the intended purpose of use and the assurance that the conditions of use will not result in an adulterated product, or one that misleads consumers.

FSIS requested that FDA advise LAMIRSA to seek regulatory guidance from FSIS, Labeling and Consumer Protection Staff, about the use of LAE in meat and poultry products. LAMIRSA should direct such an inquiry to Dr. Robert Post, Director, Labeling and Consumer Protection Staff, Office of Policy, Program, and Employee Development, Food Safety and Inspection Service, 1400 Independence Ave., S.W., Suite 602, Annex, Washington, DC 20250-3700. The telephone number for that office is (202) 205-0279 and the telefax number is (202) 205-3625.

Based on the information provided by LAMIRSA, as well as the information in GRN 000164 and other information available to FDA, the agency has no questions at this time regarding LAMIRSA's conclusion that lauramide arginine ethyl ester (LAE) 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 LAE. As always, it is the continuing responsibility of LAMIRSA to ensure that food ingredients that the firm markets 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 homepage of the Office of Food Additive Safety (on the Internet at <http://www.cfsan.fda.gov/~lrd/foodadd.html>).

Sincerely,



Laura M. Tarantino, Ph.D.

Director

Office of Food Additive Safety

Center for Food Safety

and Applied Nutrition

SEP 01 2005

cc: Dr. Robert Post, Director  
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Office of Policy, Program, and Employee Development  
Food Safety and Inspection Service  
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