U.S. Food and Drug Administration



# Food

## Agency Response Letter GRAS Notice No. GRN 000218

**CFSAN/Office of Food Additive Safety**
**June 22, 2007**

Mr. Edward A. Steele
EAS Consulting Group, LLC
1940 Duke Street
Suite 200
Alexandria, VA 22314

Re: GRAS Notice No. GRN 000218

Dear Mr. Steele:

The Food and Drug Administration (FDA) is responding to the notice, dated December 21, 2006, that you submitted on behalf of EBI Food Safety B.V. (EBI), 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 December 21, 2006, filed it on December 27, 2006, and designated it as GRAS Notice No. GRI 000218. On December 26, 2006, FDA received your letter dated December 22, 2006, clarifying the intended use.

The subject of the notice is bacteriophage P100 preparation from *Listeria innocua*. The notice informs FDA of the viev of EBI that bacteriophage P100 preparation is GRAS, through scientific procedures, as an antimicrobial to control *L. monocytogenes* in food in general, including meat and poultry products, at levels up to $10^9$ plaque forming units per gram (pfu/g) of food.

21 CFR 101.4 states that all ingredients must be declared by their common or usual name. In addition, 21 CFR 102.5 outlines general principles to use when establishing common or usual names for nonstandardized foods. Our use of "bacteriophage P100 preparation from *Listeria innocua*" or "bacteriophage P100 preparation" in this letter should not be considered an endorsement or recommendation of that term as an appropriate common or usual name for the purpose of declaring the substance in the ingredient statement of foods that contain that ingredient. Issues associated with labeling and the appropriate common or usual name of a food are the responsibility of the Office of Nutritional Products, Labeling, and Dietary Supplements in the Center for Food Safety and Applied Nutrition.

In GRN 000218, EBI incorporates by reference the conclusions of a report by a panel of individuals (EBI's GRAS panel) who evaluated the data and information in GRN 000198 on use of the bacteriophage P100 preparation in cheese. EBI considers the report of that GRAS panel as support for EBI's GRAS determination for use of bacteriophage P100 preparation in food in general, including meat and poultry. EBI considers the members of the GRAS panel it convened to review GRN 000198 to be qualified by scientific training and experience to evaluate the safety of substances added to food. In GRN 000198, EBI's GRAS panel discusses host and phage identities, method o manufacture, specifications, an estimated dietary intake for the intended use in cheese, and safety studies for the bacteriophage P100 preparation. EBI's GRAS panel also discusses a published assessment of the gene products (proteins) in bacteriophage P100 preparation to determine its potential pathogenicity, virulence, and allergenicity. EBI's GRAS panel concluded that bacteriophage P100 preparation is GRAS as an antimicrobial at levels up to $10^9$ pfu/g cheese.

For use in food in general, including meat and poultry products, EBI considers there to be no basis for setting an upper level of consumption of bacteriophage P100 preparation for safety (i.e., as is done with an acceptable daily intake). EBI considers that bacteriophage P100 preparation is composed of protein and nucleic acids like other safe sources of protein and nucleic acids, such as meat; therefore, EBI concludes there is no reason to believe that the intake of any amount of a lytic phage preparation with food would have any adverse effects on humans. EBI also concludes that lytic phage particles constitute non-toxic, naturally present components in our foods; consequently, they may be considered safe for intentional application in foods.

### Standards of Identity

In the notice, EBI cites its intention to use bacteriophage P100 preparation in several food categories, including foods for which standards of identity exist, located in Title 21 of the Code of Federal Regulations. We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity.

### Use in Meat and Poultry Products

During its evaluation of GRN 000218, 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 Mea 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 th

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 notes that EBI provided information in support of the use of bacteriophage P100 preparation on ready-to-eat (RTE) meat and poultry products. That information includes the effects of the P100 phage preparation in various foods, including hot dogs, minced meat, turkey breast and ham. Those foods were artificially contaminated with *L. monocytogenes*, then treated with bacteriophage P100 phage preparation. FSIS considers that the data show that bacteriophage 100 preparation was effective in reducing *L. monocytogenes* on these meat and poultry products.

FSIS also describes several labeling considerations regarding use of the bacteriophage P100 preparation in meat and poultry products. First, FSIS states that the ingredient should be listed as an ingredient on the label of the treated meat or poultry product.[(1)] FSIS refers to a rule that implements the use of standardized names rather than descriptive names for those standardized products (e.g., hot dogs) that permit the addition of antimicrobial agents and that the bacteriophage preparation would need to be stated in the ingredient listing on the product labeling.[(2)] FSIS indicates that when the bacteriophage P100 preparation would be applied to meat and poultry products whose standards of identity do not permit the addition of antimicrobial agents, the products would need to be descriptively named, e.g., "beef steak with an antimicrobial solutions to reduce microorganisms" and, again, the bacteriophage P100 preparation would need to be listed in the ingredient statement on the product labeling.

FSIS also mentions that the Federal meat and poultry products inspection regulations (9 CFR 424.21 (c)) limit the use of phosphates in meat and poultry to 5000 parts per million (ppm) based on the total product weight. FSIS notes that companies applying the bacteriophage preparation to meat and poultry products whose formulations contain added phosphates must ensure that the treatment does not increase the levels of phosphates beyond FSIS' current regulatory limits.

After reviewing the data on organoleptic changes (i.e., color, odor, and taste) associated with use of bacteriophage P100 preparation under the proposed conditions of use, FSIS concludes that the use of this phage preparation on RTE meat and poultry products would not have any adverse effects on the organoleptic properties. Consequently, FSIS does not have any objection to the use of bacteriophage P100 preparation, under the conditions described in the notice, for use as an antimicrobial agent on various non-standardized RTE meat and poultry products and standardized meat and poultry products that permit the use of any safe and suitable antimicrobial agent.

Further questions regarding use in meat and poultry products should be directed 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.

## Conclusion

Based on the information provided by EBI, as well as other information available to FDA, the agency has no question at this time regarding EBI's conclusion that bacteriophage P100 preparation is GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding bacteriophage P100 preparation. As always, it is the continuing responsibility of EBI 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 responding to GRN 000218, as well as a copy of the information in this notice that conforms to the information in the proposed GRAS exemption claim (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

cc: Dr. Robert Post, Director
Labeling and Consumer Protection Staff
Office of Policy, Program and Employee Development
Food Safety and Inspection Service
1400 Independence Ave., SW, Suite 602, Annex
Washington, DC 20250-3700

[(1)]FSIS considers the use of the bacteriophage preparation to be inconsistent with the definition of a processing aid in 21 CFR 101.100(a)(3)(ii).

[(2)]On April 29, 2003, FSIS published a direct final rule in the *Federal Register* entitled "Approving Ingredients Used in the Production of Meat and Poultry Products: Use of Any Safe and Suitable Binder or Antimicrobial Agent in Meat and Poultry Products with Standards of Identity or Composition."

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