Steven Hagens, Ph.D.
Chief Scientific Officer
Micreos B.V.
Nieuwe Kanaal 7P
6709 PA Wageningen
The NETHERLANDS

Re: GRAS Notice No. GRN 000757

Dear Dr. Hagens:

The Food and Drug Administration (FDA, we) completed our evaluation of Micreos B.V.'s (Micreos) supplement to GRN 000757. We received the supplement on April 3, 2019. The supplement addresses additional uses for a preparation containing two bacteriophages (EP335 and ER75) specific to *Escherichia coli* O157 (*E. coli* O157 bacteriophage preparation). Micreos submitted additional information on September 27, 2019, to clarify the possible intervention strategies.

We previously responded to GRN 000757 on August 3, 2018. We stated that we had no questions at that time regarding Micreos's conclusion that *E. coli* O157 bacteriophage preparation is GRAS for use as an antimicrobial at up to 10^9 plaque-forming units (PFU)/g of beef (on beef carcasses, primals, subprimal cuts, and trimmings) to control *E. coli* O157.

In the supplement received April 3, 2019, Micreos informs us of its view that *E. coli* O157 bacteriophage preparation is GRAS for use as an antimicrobial on fresh vegetables to control *E. coli* O157 at an application rate of up to 10^9 PFU/g of food.

The changes in the intended uses do not affect the identity, method of manufacture, specifications, and safety of the product. However, the estimated dietary exposure to *E. coli* O157 phage preparation based on consumption data for the food categories of its intended use is adjusted to reflect the uses added in this supplement. In addition to the estimated dietary exposure from beef, Micreos bases its estimate on the intended use level of *E. coli* O157 phage preparation on vegetables, the estimated average *per capita* daily vegetables consumption, and the assumption that all vegetables consumed are treated with *E. coli* O157 phage preparation. Micreos estimates dietary exposure at 44.8 µg/person/day (2.7×10^{11} PFU/day).

Micreos provides data demonstrating the antimicrobial effects of the *E. coli* O157 bacteriophage preparation when applied to the surface of vegetable samples inoculated with *E. coli* O157.

Based on the totality of the data and information available, Micreos concludes that *E. coli* O157 bacteriophage preparation is GRAS for its intended use on fresh vegetables.

Some Uses May Require Regulatory Actions by the United States Environmental Protection Agency (EPA)

Antimicrobial agents used on preharvest and raw agricultural commodities may require registration as pesticides with EPA under the Federal Insecticide, Fungicide, and Rodenticide Act. FDA's evaluation of this supplement does not relieve the obligation to register *E. coli* O157 bacteriophage preparation as a pesticide for uses regulated by EPA. For information about the regulatory status of this product when used as a pesticide, please contact EPA's Office of Pesticide Products, Antimicrobial Division.

Section 301(ll) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ll)(1)-(4) applies. In our evaluation of Micreos' supplement concluding that *E. coli* O157 bacteriophage preparation is GRAS under its intended conditions of use, we did not consider whether section 301(ll) or any of its exemptions apply to foods containing *E. coli* O157 bacteriophage preparation. Accordingly, our response should not be construed to be a statement that foods containing *E. coli* O157 bacteriophage preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Micreos provided, as well as other information available to FDA, we have no questions at this time regarding Micreos' conclusion that *E. coli* O157 bacteriophage preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *E. coli* O157 bacteriophage preparation is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient manufacturers and food producers are responsible for ensuring that marketed products are safe and compliant with all applicable legal and regulatory requirements.

In accordance with 21 CFR 170.275(b)(2), the text of this letter responding to the supplement to GRN 000757 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2019.10.25 12:20:12 -04'00'

Susan Carlson, Ph.D.
Director
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