Robin Peterson
Micreos B.V.
Nieuwe Kanaal 7P
6709 PA Wageningen
THE NETHERLANDS

Re: GRAS Notice No. GRN 000468

Dear Ms. Peterson:

The Food and Drug Administration (FDA, we) completed our evaluation of Micreos B.V.'s (Micreos) supplement to GRN 000468. We received the supplement on November 20, 2020. The supplement addresses additional uses for the subject of GRN 000468. Micreos submitted clarifying information on March 11, 2021.

We previously responded to GRN 000468 on December 23, 2013. We stated that we had no questions at that time regarding Micreos' conclusion that a preparation containing two bacteriophages (phage), FO1a and S16, specific to *Salmonella* serovars (*Salmonella* phage preparation) is GRAS for use as an antimicrobial on certain pork and poultry products at levels up to 10^8 plaque forming units (PFU)/g of food. Subsequently, on December 2, 2016, FDA responded with no questions to a supplement to GRN 000468 from Micreos, received May 17, 2016, for use of *Salmonella* phage preparation as an antimicrobial on beef and vegetables at levels up to 10^8 PFU/g of food.

In the supplement dated November 17, 2020, Micreos informed us of its view that the additional uses of *Salmonella* phage preparation are GRAS, through scientific procedures, for use as an antimicrobial on fresh and saltwater seafood (excluding Siluriformes (catfish); as clarified on March 11, 2021) at levels up to 10^8 PFU/g of food.

Micreos states that the identity and method of manufacture are the same as discussed in GRN 000468. Micreos estimates the dietary exposure to *Salmonella* phage preparation for the United States (U.S.) population based on per capita consumption data from the U.S. Department of Agriculture's Economic Research Services. Based on the intended uses in red meats, poultry, vegetables, and fish as described in the supplement, Micreos estimates that people will consume 4×10^{10} PFU/person (p)/d (or 6 µg/p/d).[1] Micreos conducted a literature review through October 2020 and summarizes the published literature evaluating the use of phage to control for the presence of

[1] FDA independently estimated eaters-only dietary exposure to *Salmonella* phage preparation for the U.S population aged 2 years and older for the intended uses using the most recent National Health and Nutrition Examination Survey (NHANES 2013-2016) data to be 4 µg/p/d at the mean and 7 µg/p/d at the 90th percentile, respectively.

Salmonella serovars on seafood. Micreos provides data demonstrating the antimicrobial effects of *Salmonella* phage preparation when applied to fresh and saltwater fish (tilapia and cod, respectively) at 10^8 PFU/cm^2 of food.

Based on the data and information presented in the supplement, Micreos concludes that *Salmonella* phage preparation is GRAS for its intended use.

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 *Salmonella* phage 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 *Salmonella* phage preparation. Accordingly, our response should not be construed to be a statement that foods containing *Salmonella* phage 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 *Salmonella* phage preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *Salmonella* phage 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 000468 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2021.04.06 12:00:58 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
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