Alexander Sulakvelidze, Ph.D.
Intralytix, Inc.
8681 Robert Fulton Drive
Columbia, MD 21046

Re: GRAS Notice No. GRN 000435

Dear Dr. Sulakvelidze:

The Food and Drug Administration (FDA, we) completed our evaluation of Intralytix, Inc.'s (Intralytix) supplement to GRN 000435. We received the supplement on January 4, 2021. The supplement addresses an increased use level for the subject of GRN 000435. Intralytix submitted clarifying information on March 6, 2021, which included an updated estimate of dietary exposure.

We previously responded to GRN 000435 on February 22, 2013. We stated that we had no questions at that time regarding Intralytix's conclusion that a preparation consisting of six bacterial monophages specific to *Salmonella enterica* (monophage cocktail) is GRAS for the intended use as an antimicrobial in certain poultry products, fish, shellfish, and fresh and processed fruits and vegetables at 10^7 plaque-forming units (PFU)/g of food. On February 13, 2015, FDA responded with no questions to a supplement to GRN 000435 from Intralytix, dated October 28, 2014, for use of monophage cocktail as an antimicrobial on raw poultry in general at 10^7 PFU/g of food. Subsequently, on November 15, 2019, FDA responded with no questions to a supplement to GRN 000435 from Intralytix, dated January 29, 2019, for use of monophage cocktail as an antimicrobial in ready-to-eat and raw red meat carcasses, subprimals, and trimmings at 10^7 PFU/g of food.

In the supplement received January 4, 2021, Intralytix informs us of its view that monophage cocktail is GRAS, through scientific procedures, for use as an antimicrobial in certain poultry products, fish, shellfish, and fresh and processed fruits and vegetables; raw poultry in general; and ready-to-eat and raw red meat carcasses, subprimals and trimmings at up to 10^8 PFU/g of food.

Intralytix states that the identity and the method of manufacture are the same as discussed in GRN 000435. Intralytix estimates the dietary exposure to monophage cocktail for the US population based on the data from the Food Availability Data System by the Economic research Service of United States Department of Agriculture (accessed December 2020). Monophage cocktail is intended for use at a maximum level of 1×10^8 PFU/g in certain poultry products, fish, shellfish, and fresh and processed fruits and vegetables; raw poultry in general; and ready-to-eat and raw red meat carcasses, subprimals, and trimmings. Based on the food disappearance data of these food

categories, Intralytix estimates the total daily consumption of monophage cocktail to be 39.9 µg/person (p)/d, resulting in a daily dietary exposure of 13.3 µg/kg. Intralytix estimates the daily dietary exposure to endotoxin, sodium, and potassium to be negligible at the use level of monophage cocktail. Intralytix conducted a literature review through December 2020 and concludes that the safety of bacteriophage continues to be confirmed and that there is an absence of adverse effects.

Based on the data and information presented in the supplement, Intralytix concludes that monophage cocktail is GRAS for its intended use.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of this supplement to GRN 000435, we coordinated with the Food Safety and Inspection Service (FSIS) of the United States Department of Agriculture. Under the Federal Meat Inspection Act, the Poultry Products Inspection Act, and the Egg Products Inspection Act, FSIS determines the efficacy and suitability of ingredients used in meat, poultry, and egg products, and prescribes safe conditions of use. Suitability relates to the ingredient's effectiveness in performing its intended technical effect and the assurance that the ingredient's use will not result in products that are adulterated or misleading for consumers.

FSIS has completed its review and has no objection to the use of monophage cocktail, as an antimicrobial agent in ready-to-eat and raw poultry products, ready-to-eat and raw red meat carcasses, subprimals and trimmings up to a level of 1×10^8 PFU/g of food.

FSIS requested that we advise you to seek regulatory guidance from its Risk Management and Innovations Staff (RMIS) about the use of monophage cocktail in meat, poultry, and egg products. You should direct such an inquiry to Dr. Melvin Carter, Director, RMIS, Office of Policy and Program Development, FSIS by email at Melvin.Carter@fsis.usda.gov.

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 Intralytix's supplement concluding that monophage cocktail 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 monophage cocktail. Accordingly, our response should not be construed to be a statement that foods containing monophage cocktail, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Intralytix provided, as well as other information available to FDA, we have no questions at this time regarding Intralytix's conclusion that monophage cocktail is GRAS under its intended conditions of use. This letter is not an affirmation that monophage cocktail 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 000435 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2021.06.28 15:41:23 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

cc: Melvin Carter, Ph.D.
Director
USDA/FSIS/OPPD/RMIS
Stop Code 3782, Patriots Plaza III
1400 Independence Ave. SW
Washington, DC 20250-3700