Joelle Woolston
Intralytix, Inc.
8681 Robert Fulton Drive
Columbia, MD 21046

Re: GRAS Notice No. GRN 000435

Dear Ms. Woolston:

The Food and Drug Administration (FDA, we) completed our evaluation of Intralytix, Inc.'s (Intralytix) supplement to GRN 000435. We received the supplement on April 17, 2023. The supplement addresses additional uses for the subject of GRN 000435. Intralytix submitted clarifying information on August 14, 2023, which included clarification regarding the specifications, results from three non-consecutive batch analyses, a revised dietary exposure assessment, and an explanation of the provided efficacy studies.

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 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 to a supplement to GRN 000435 dated October 28, 2014, stating that we had no questions at that time regarding Intralytix's conclusion that monophage cocktail is GRAS for use as an antimicrobial on raw poultry in general at 10^7 PFU/g of food. Subsequently, on November 15, 2019, FDA responded to a supplement to GRN 000435 dated January 29, 2019, stating that we had no questions at that time regarding Intralytix's conclusion that monophage cocktail is GRAS for use as an antimicrobial in ready-to-eat and raw red meat carcasses, subprimals, and trimmings at 10^7 PFU/g of food. Finally, on June 28, 2021, FDA responded to a supplement to GRN 000435 dated December 29, 2020, stating that we had no questions at that time regarding Intralytix's conclusion that monophage cocktail is GRAS 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.

In the supplement dated April 17, 2023, Intralytix informs us of its view that monophage cocktail is GRAS, through scientific procedures, for use as an antimicrobial at up to 10^8 PFU/g of food in grain and grain products.

Intralytix states that the identity, the method of manufacture, and the specifications are

the same as described in GRN 000435. Intralytix estimates the dietary exposure to monophage cocktail based on the intended maximum use level of 1 x 10^8 PFU/g of food and the average per capita daily consumption of all foods in which monophage cocktail could be used, estimated using data from the Food Availability (Per Capita) Data System (Economic Research Service, U.S. Department of Agriculture). Intralytix estimates the dietary exposure to monophage cocktail from all uses of monophage cocktail to be 46.7 µg/person/d.

Intralytix conducted a literature review through April 2023 and concludes that the safety of bacteriophage continues to be confirmed and that there is an absence of adverse effects. To support use in grain and grain products, Intralytix's supplement includes supporting data examining the efficacy of monophage cocktail in wheat grain.[1]

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

Standards of Identity

In the supplement, Intralytix states its intention to use monophage cocktail in several food categories, including foods for which standards of identity exist, located in Title 21 of the CFR. 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.

Allergen Labeling

The Federal Food, Drug, and Cosmetic Act (FD&C Act) requires that the label of a food that is or contains an ingredient that contains a "major food allergen" declare the allergen's presence (section 403(w)). The FD&C Act defines a "major food allergen" as one of nine foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, soybeans, and sesame) or a food ingredient that contains protein derived from one of those foods. Monophage cocktail may require labeling under the FD&C Act because it may contain protein derived from soy. Questions about petitions or notifications for exemptions from the food allergen labeling requirements should be directed to the Division of Food Ingredients in the Office of Food Additive Safety.

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[1] Intralytix explains that the concept for the efficacy studies is that monophage cocktail can be applied during the wheat tempering stage to significantly reduce *Salmonella* contamination of wheat grain which would then lead to decreased (or eliminated) *Salmonella* levels during milling. Intralytix states that efficacy studies with enumeration of *Salmonella* serovars in flour were not performed for monophage cocktail; however, were performed in a commercial milling facility for the technically equivalent *Escherichia coli* phage preparation that is the subject of GRN 000834 (data presented in the April 17, 2023, supplement to GRN 000834). Intralytix notes that similar efficacy studies with *Salmonella* serovars were not possible, because a non-pathogenic surrogate *Salmonella* strain was not available and introducing a pathogenic *Salmonella* strain into a working mill was not feasible. Intralytix states that, based on the similar efficacy results presented in the supplements to GRNs 000435 and 000834, both dated April 17, 2023, monophage cocktail will provide similar efficacy as *E. coli* phage preparation on wheat grains subjected to milling. We evaluated the April 17, 2023, supplement to GRN 000834, and responded in a letter dated January 12, 2024, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

Questions related to food labeling in general should be directed to the Office of Nutrition and Food Labeling in the Center for Food Safety and Applied Nutrition.

Section 301(ll) of the 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: 2024.01.17 16:42:27 -05'00'

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