



Tyler Homer  
OmniLytics, Inc.  
9075 South Sandy Parkway  
Sandy, UT 84070

Re: GRAS Notice No. GRN 000827

Dear Mr. Homer:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000827. We received the notice from OmniLytics Inc. (OmniLytics) on October 4, 2018 and filed it on February 12, 2019. In amendments dated March 13, May 30, and July 23, 2019, OmniLytics provided additional information on the intended uses, antimicrobial effects, and conditions of use of the product.

The subject of the notice is a preparation containing three bacterial monophages (MLF4, OLB35 and OLB145) specific to *Escherichia coli* (*E. coli* phage preparation). The preparation is intended for use as an antimicrobial agent to control specific *E. coli* serotypes on, fruits, vegetables, eggs, fish (excluding Siluriformes), and shellfish when applied to food surfaces at up to  $10^8$  plaque-forming units (PFU)/g food.<sup>1</sup> The notice informs us of OmniLytics's view that these uses of the *E. coli* phage preparation are GRAS through scientific procedures.

OmniLytics describes the *E. coli* phage preparation as an opalescent liquid consisting of three monophages (MLF4, OLB35, and OLB145) that are produced and purified separately and mixed in equal concentrations. The *E. coli* phage preparation has a minimum titer of  $10^{10}$  PFU/mL. OmniLytics states that this suspension is a concentrated form that is diluted with water at the application sites to provide a maximum application rate of  $10^8$  PFU/g of food.

OmniLytics describes the method of manufacture for *E. coli* phage preparation. The monophages are produced using nonpathogenic bacterial hosts (*E. coli* 11-1178D for monophage MLF4, *E. coli* 43888™ for OLB35 and *E. coli* 12-799F for OLB145). OmniLytics states that *E. coli* 43888™ is a commercially available strain that does not produce Shiga toxins stx1 and stx2, while *E. coli* 11-1178D and 12-799F were from OmniLytics's own library and were verified to be Shiga toxin negative. The production hosts were sensitive to all antibiotics tested apart from penicillin. OmniLytics states that all materials used in the manufacture of *E. coli* phage preparation are food grade and the final preparation does not contain any known allergens.

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<sup>1</sup> In an amendment dated July 23, 2019, the OmniLytics excluded the use of *E. coli* phage preparation on products under the jurisdiction of the United States Department of Agriculture (USDA).

The three monophages are produced separately using aerobic fermentation. Each host bacterium is grown to a desired concentration before each monophage is added at a predetermined multiplicity of infection. After fermentation, the culture is filtered, washed, and concentrated by tangential flow filtration. The concentrated product is filter-sterilized and diluted to a titer of  $10^{10}$  PFU/mL. The individual monophage solutions are then blended together, filter-sterilized, packaged, and refrigerated.

OmniLytics describes specifications for *E. coli* phage preparation that include an analysis of the titer ( $>10^{10}$  PFU/mL), identity (using PCR analysis and matching the results with reference profiles), and sterility (no bacterial growth after 7 days). OmniLytics discusses the results from three batches of the *E. coli* phage preparation that examine the physical and chemical composition.

OmniLytics estimates the dietary exposure to *E. coli* phage preparation based on consumption data for the food categories of its intended use. OmniLytics estimates that the average *per capita* consumption of these food categories is 727 g/person/day based on data from the Economic Research Service of the USDA (2017). To estimate dietary exposure to the *E. coli* phage preparation, OmniLytics assumes that all the relevant foods are treated with *E. coli* phage preparation at applied at a rate of  $10^8$  PFU/g of food. This scenario results into a dietary exposure of  $5.7 \times 10^{10}$  PFU/person/day.<sup>2</sup>

OmniLytics discusses the safety of use of *E. coli* phage preparation. OmniLytics states that phages are ubiquitous in the environment and the human body. OmniLytics also states that humans consume phages via various foods; hence, phages are found in the human digestive system. OmniLytics states that the biology of lytic phages has been extensively studied and documented. OmniLytics notes that most lytic phages display very limited host range even among specific bacteria and bacteria strains, and lytic phages have a reduced potential for bacterial development of resistance. Citing several published studies, OmniLytics states that the consumption of lytic phages is harmless to humans. In one such study cited by OmniLytics, there were no observed adverse effects when healthy adult human volunteers ingested *E. coli*-specific phages. OmniLytics reports that the proposed exposure of its *E. coli* phage preparation is equivalent to similar phage products that are already on the market.

OmniLytics provides data from its own studies demonstrating the antimicrobial effects of *E. coli* phage preparation when applied to a variety of foods (e.g., spinach, crab, pre-cut apples, eggs, and salmon) at  $10^8$  PFU/g food.

Based on the totality of information discussed above, OmniLytics concludes that *E. coli* phage preparation is GRAS for its intended use.

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<sup>2</sup> Because of the amendment excluding use in products under USDA jurisdiction, the dietary exposure estimates to the *E. coli* phage preparation change to 565 g/person/day and the exposure to the monophages change to  $5.7 \times 10^{10}$  from  $7.3 \times 10^{10}$  PFU/person/day.

## Standards of Identity

In the notice, OmniLytics states its intention to use *E. coli* phage preparation 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.

## 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 OmniLytics's notice concluding that the *E. coli* 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 *E. coli* phage preparation. Accordingly, our response should not be construed to be a statement that foods containing *E. coli* phage preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

## Conclusions

Based on the information that OmniLytics provided, as well as other information available to FDA, we have no questions at this time regarding OmniLytics's conclusion that *E. coli* phage preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *E. coli* 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 GRN 000827 is accessible to the public at [www.fda.gov/grasnoticeinventory](http://www.fda.gov/grasnoticeinventory).

Sincerely,

Susan J.  
Carlson -S

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Susan Carlson, Ph.D.  
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