



Edith Chow, PhD
SK8 Biotechnologies Inc.
185 Pony Dr.
Newmarket, Ontario, L3Y 7B5
CANADA

Re: GRAS Notice No. GRN 001304

Dear Dr. Chow:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001304. We received SK8 Biotechnologies Inc. (SK8)'s GRAS notice on September 17, 2025, and filed it on April 6, 2026. SK8 submitted amendments to the notice on June 10, 2026, June 17, 2026, June 25, 2026, June 30, 2026, August 25, 2026, and September 15, 2026, clarifying the identity, manufacturing process, specifications, analytical methods, intended uses, dietary exposure, safety information and antimicrobial efficacy and suitability data.

The subject of the notice is a bacteriophage (phage) preparation specific to *Listeria monocytogenes* (*Listeria* phage preparation) for use as an antimicrobial on dairy, fruits, vegetables, shell eggs, nuts, fish (excluding Siluriformes), ready-to-eat meats and fish, raw beef, and raw poultry at levels up to 2×10^8 plaque forming units (PFU)/g of food, excluding use in infant formula, foods for infants and toddlers, and alcoholic beverages. The notice informs us of SK8's view that these uses of *Listeria* phage preparation are GRAS through scientific procedures.

SK8 describes the *Listeria* phage preparation as a clear translucent liquid that consists of a minimum of three out of eight strictly lytic, double-stranded DNA phage specific to a wide range of *Listeria* isolates. SK8 explains that the phage was characterized using whole genome sequencing. SK8 states that the *Listeria* phage preparation shows lytic activity against 91% of *L. monocytogenes* strains and 73% of the non-*monocytogenes* strains.

SK8 describes the manufacturing process of *Listeria* phage preparation. SK8 states that each of the phages is produced individually and then mixed prior to use on food. The individual phages are produced using a non-pathogenic and non-toxigenic bacterial host (*L. innocua* SK8_B0142). SK8 states that the *L. innocua* host strain is not genetically engineered and does not produce undesirable secondary metabolites. SK8 describes that the aerobic fermentation process occurs in a contained, sterile environment. The *L. innocua* host strain is grown to a specific concentration, and the bacteriophage is added at a predetermined multiplicity of infection and fermented for a pre-defined duration.

SK8 states that, after the fermentation process is complete, the culture is centrifuged and subjected to microfiltration. The resulting phages are washed with a magnesium sulfate solution to remove the fermentation broth and other contaminants, such as host proteins. SK8 states that none of the materials used during the manufacturing process are derived from major allergens. SK8 states that *Listeria* phage preparation is manufactured in accordance with good manufacturing practices and that all raw materials and processing aids are food-grade and are used in accordance with applicable U.S. regulations, are GRAS for the intended use, or are the subject of an effective food contact notification.

SK8 provides specifications for *Listeria* phage preparation, including concentration ($> 10^{11}$ PFU/mL), and limits for heavy metals, including lead (< 0.01 mg/L), and bacterial sterility (no growth after 7 days). SK8 provides the results from the analyses of three non-consecutive batches to demonstrate that *Listeria* phage preparation can be manufactured to meet the specifications. SK8 states that a *Listeria* phage preparation is stable for one year when stored at 2-8 °C in a dark environment.

SK8 estimates the dietary exposure to *Listeria* phage preparation based on the maximum use level of 2×10^8 PFU/g of food and the average per capita food availability reported in the Food Availability (Per Capita) Data System (Economic Research Service, U.S. Department of Agriculture, 2025). SK8 estimates the dietary exposure to *Listeria* phage preparation from the intended uses to be 21 µg/person/d.

SK8 discusses the safety of phages in general, stating that phages are abundant in the environment. SK8 notes that phages are found in human and animal guts and are consumed in various foods. SK8 states that the use of lytic phages as antimicrobials to reduce the loads of *L. monocytogenes* has been demonstrated in different foods. SK8 states that genomic and phenotypic analyses of the phages in *Listeria* phage preparation confirm that they are strictly lytic and do not contain a functional portion of any of the toxin-encoding sequences. SK8 conducted a literature search through September 2025 and states that no new information contradicting their GRAS conclusion was identified.

SK8 provides data demonstrating the antimicrobial effects of *Listeria* phage preparation when applied to foods such as Romaine lettuce, apple slices, Mozzarella cheese, raw beef, smoked salmon, shell eggs, whole sausages, whole almonds, skin-on chicken drumsticks, cooked ham, soft cheese, and desalted cod at an application titer of 2×10^{10} PFU/cm².

Based on data and information provided in the submission, SK8 concludes that *Listeria* phage preparation is GRAS for its intended use.

Standards of Identity

In the notice, SK8 states its intention to use *Listeria* 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.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 001304, 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 a phage cocktail containing at least three of the *Listeria* phage preparation as an antimicrobial to control *Listeria* spp. at rates not to exceed 2×10^8 PFU/g of food for RTE red meat and poultry, raw intact red meat, raw intact poultry, and shell eggs. FSIS would consider the substance a processing aid that does not require a labeling statement under the accepted conditions of use.

FSIS requested that we advise you to seek regulatory guidance from its Risk Management and Innovations Staff (RMIS) about the use of *Listeria* phage preparation in meat, poultry, and egg products. You should direct such an inquiry to Selena Kremer-Caldwell, Acting Director, RMIS, Office of Policy and Program Development, FSIS by email at selena.kremer-caldwell@usda.gov.

Section 301(ll) of the Federal Food, Drug, and Cosmetic (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 SK8's notice concluding that *Listeria* 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 *Listeria* phage preparation. Accordingly, our response should not be construed to be a statement that foods containing *Listeria* phage preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that SK8 provided, as well as other information available to FDA, we have no questions at this time regarding SK8's conclusion that *Listeria* phage preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *Listeria* 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 001304 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

SUSAN J.

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Susan J. Carlson, Ph.D.
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