



Michelle Tessier
Fumoir Grizzly Inc.
159 d'Amsterdam street,
Saint-Augustin-De-Desmaures
Quebec, CANADA
G3A 2V5

Re: GRAS Notice No. GRN 001066

Dear Ms. Tessier:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001066. We received Fumoir Grizzly Inc.'s (Fumoir)'s notice on April 13, 2022 and filed it on August 5, 2022. Fumoir submitted amendments to the notice on February 6, 2023 and March 6, 2023 discussing manufacturing, the mechanism of microbial control, analytical methods, dietary exposure, and potential pathogenicity.

The subject of the notice is *Carnobacterium divergens* strain M35 (*C. divergens* M35) for use as an antimicrobial agent at levels up to 10^6 colony forming units (CFU)/g of fresh, frozen, or smoked fish products (excluding catfish/Siluriformes) to inhibit the growth of *Listeria monocytogenes*.¹ The notice informs us of Fumoir's view that these uses of *C. divergens* M35 are GRAS through scientific procedures.

Fumoir describes *C. divergens* M35 as a yellowish powder. Fumoir states that *C. divergens* M35 is a nonpathogenic, nontoxicogenic bacterium that can be described as a non-motile, Gram-positive, non-spore forming, rod that grows in short chains and is catalase and oxidase negative. The strain was isolated from frozen smoked mussels originating from the waters of the St-Lawrence River in Gaspé, Quebec, Canada and was deposited at the International Depository Authority of Canada in Winnipeg, Manitoba under the designation ADI 050404-01. Fumoir discusses the results of the phenotypic and genotypic characterization used to confirm the strain identity and states that the strain does not produce secondary amines. Fumoir states that *C. divergens* M35 produces the bacteriocin divergicin which can inhibit the growth of *L. monocytogenes*.

Fumoir describes the manufacture of *C. divergens* M35 by fermentation of a pure culture under controlled conditions. Upon completion of fermentation, the culture is either freeze dried or spray dried and then vacuum-packed in oxygen impermeable packaging. Fumoir states that *C. divergens* M35 is manufactured under current good

¹ Fumoir states that *C. divergens* M35 is not intended for use products under the jurisdiction of the United States Department of Agriculture.

manufacturing practices using food-grade materials. Fumoir states that all raw materials and processing aids are used in accordance with existing U.S. regulations, are GRAS for their intended use, or are the subject of an effective food contact notification. Fumoir provides specifications for *C. divergens* M35 that include limits for heavy metals, including lead (≤ 0.1 mg/kg) and for microorganisms including, *Salmonella* serovars (absent in 25 g), *L. monocytogenes* (absent in 25 g), *Escherichia coli* O157:H7 (absent in 25 g) and *Staphylococcus aureus* (<25 CFU/ g). Fumoir provides the results from the analyses of four nonconsecutive batches to demonstrate that *C. divergens* M35 is manufactured to conform with the provided specifications.

Fumoir estimates dietary exposure to *C. divergens* M35 using 2020 per capita consumption data from the NOAA Fisheries for fresh and frozen finfish of 8.3 pounds. Fumoir doubled this amount to estimate a pseudo 90th percentile dietary exposure to *C. divergens* M35. Fumoir estimates the per capita dietary exposure to be 1.3×10^7 CFU/p/d at the mean and 2.06×10^7 CFU/p/d at the pseudo 90th percentile based on a use level of *C. divergens* M35 of 10^6 CFU/g of fish. Fumoir also notes that *C. divergens* M35 can grow on fish and estimates dietary exposure using an upper limit for *C. divergens* M35 of 10^9 CFU/g of fish. This results in a per capita dietary exposure of 1.3×10^{10} CFU/p/d at the mean and 2.06×10^{10} CFU/p/d at the pseudo 90th percentile.

Fumoir performed a literature search and discusses the safety of bacteriocins. Fumoir states that *C. divergens* is already part of the natural gut microbiota of humans and that *C. divergens* is found on meat, fish, dairy products, and in water. Fumoir concludes that humans and animals have been extensively exposed to *C. divergens* and that ingestion of bacteriocins would not have any deleterious effect on the human microbiota and would not induce any allergenic or toxic effect for humans.

Fumoir provided data that demonstrates that treatment of *L. monocytogenes* inoculated fresh tuna and cold-smoked salmon with *C. divergens* M35 was an effective treatment to reduce and control subsequent growth of *L. monocytogenes*.

Based on the data and information, Fumoir concludes that *C. divergens* M35 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 Fumoir's notice concluding that *C. divergens* M35 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 *C. divergens* M35. Accordingly, our response should not be construed to be a statement that foods containing *C. divergens* M35, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Fumoir provided, as well as other information available to FDA, we have no questions at this time regarding Fumoir's conclusion that *C. divergens* M35 is GRAS under its intended conditions of use. This letter is not an affirmation that *C. divergens* M35 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 001066 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J.
Carlson -S

Digitally signed by Susan J.
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Date: 2023.04.26 10:26:04
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