Frederick A. Stearns
Keller and Heckman LLP
1001 G Street, NW
Suite 500W
Washington, DC 20001

Re: GRAS Notice No. GRN 001117

Dear Mr. Stearns:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001117. We received the notice that you submitted on behalf of The Better Meat Co. (BMC) on October 4, 2022 and filed it on July 8, 2023. BMC submitted amendments to the notice on October 2, 2023, October 30, 2023, December 12, 2023, January 24, 2024, January 29, 2024, March 14, 2024, April 24, 2024, and June 25, 2024 further clarifying medium components, analytical methods and specifications, dietary exposure estimates, RNA content, ingredient composition for labeling, and human consumption and tolerability.

The subject of the notice is mycelial biomass from *Neurospora crassa* Bstr 26 (fungal protein) for use as an ingredient and a source of protein in foods at the maximum use levels as specified in Table 1.[1] The notice informs us of BMC's view that these uses of fungal protein are GRAS through scientific procedures.

Table 1. Proposed uses and use levels for *N. crassa* fungal protein.

Food Category	Maximum use level (%)
Ground, minced, chopped meat (including pork), poultry, and seafood	50
Plant-based meat alternatives	90
Dairy analogs (milk alternatives, imitation cheese, cream cheese substitutes, coffee creamer, frozen desserts, whipped topping, and yogurt alternatives)	50

Our use of the terms "fungal protein" and "mycelial biomass from *N. crassa* Bstr 26" in this letter is not our recommendation of that term as an appropriate common or usual name for declaring the substance in accordance with FDA's labeling requirements. Under 21 CFR 101.4, each ingredient must be declared by its common or usual name. In addition, 21 CFR 102.5 outlines general principles to use when establishing common or usual names for non-standardized foods. Issues associated with labeling and the common or usual name of a food ingredient are under the purview of the Office of

[1] BMC states that the fungal protein is not intended to be used in infant formula.

Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied Nutrition (CFSAN). The Office of Food Additive Safety (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "fungal protein."

BMC provides information on the identity and composition of fungal protein. BMC states that fungal protein contains 30% solids and can be dried to a product that contains approximately 93% solids. On a dry weight basis, the fungal protein is approximately 40-50% protein, approximately 30% fiber, 8% non-fiber carbohydrates, 4% fat, 7% ash and 5-7 % moisture.

BMC states that the production organism has been deposited in the International Depositary Authority and assigned the identifier NRRL 68076. BMC states that fungal protein is manufactured by fermentation under controlled conditions from a wild-type, unmodified *N. crassa* Bstr 26. After the fermentation is complete, the mycelium is dewatered to produce a moist cake and then further dehydrated and inactivated by heat treatment. BMC states that fungal protein will be manufactured in both dry and rehydrated forms. BMC states that fungal protein is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids are food grade and approved for their respective uses in accordance with an appropriate U.S. regulation or are GRAS for that use. Finally, BMC states that the fungal protein fermentation media is free of major allergens.

BMC provides specifications for fungal protein that include protein content (> 40% on dry matter basis (DM)), and limits for ash (<10% DM), moisture (<11% DM), total arsenic (<0.1 mg/kg DM), cadmium (<0.1 mg/kg), mercury (<0.1 mg/kg DM), lead (<0.1 mg/kg DM) and microorganisms. BMC provides the results from the analyses of three non-consecutive batches to demonstrate that fungal protein can be manufactured to meet the specifications. BMC states that *N. crassa* has not been reported to produce mycotoxins and provided results from genetic analysis and analytical studies to demonstrate that the *N. crassa* mycelium does not contain mycotoxins.

Using food consumption data from the 2015-2018 National Health and Examination Survey (NHANES), BMC estimates the eaters-only dietary exposure to fungal protein (dry weight basis) from the proposed uses to be 18.5 g/p/d at the mean and 40.2 g/p/d at the 90th percentile for the U.S. population aged 2 years and older. BMC also estimates that the highest amount of fungal protein will be consumed by adults aged 19 years old older with an estimated dietary exposure of 18.9 g/p/d at the mean and 41.5 g/p/d at the 90th percentile. Additionally, BMC estimates a 90th percentile dietary exposure to total RNA from fungal protein to be 183 mg/p/d for adults aged 19 and older.

BMC discusses publicly available data and information sourced from a literature review in support of the safety of fungal protein as a food ingredient. These data include, but were not limited to, traditional and non-traditional oral toxicity studies in multiple animal species, and *in vitro* genotoxicity studies. BMC emphasizes a published 90-day repeat oral toxicity study in rats, performed under OECD guidelines, where fungal protein was used as the test article. From the totality of these data, BMC concludes that fungal protein is non-genotoxic and notes that no treatment-related adverse effects were

observed in rats up to the maximum dose tested.[2] Further, BMC discusses the safety of dietary exposure to total RNA from fungal protein, noting that both dietary exposure to nucleic acids and total RNA content in the final product are below levels that would raise concern.[3] Regarding potential allergenicity concerns, BMC discusses a published combined literature review and bioinformatics analysis for isolated *N. crassa* mycelium as a food ingredient, from which they conclude that oral consumption of the fungal protein is unlikely to cause an allergic reaction in consumers. Further, BMC states that *N. crassa* fungal protein is well tolerated in human consumption trials, where no reports of major gastrointestinal issues, such as diarrhea or vomiting were observed. BMC concludes that *N. crassa* fungal protein has no known tolerability concerns in humans.

Based on the totality of the data and information, BMC concludes that fungal protein is GRAS for its intended use.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, & Cosmetic Act (FD&C Act), a food is misbranded if its labeling is false or misleading in any way. Section 403(r) of the FD&C Act lays out the statutory framework for labeling claims characterizing a nutrient level in a food or the relationship of a nutrient to a disease or health-related condition (also referred to as nutrient content claims and health claims). If products containing fungal protein bear any nutrient content or health claims on the label or in labeling, such claims are subject to the applicable requirements and are under the purview of the ONFL in CFSAN. OFAS did not consult with ONFL on this issue or evaluate any information in terms of labeling claims. Questions related to food labeling should be directed to ONFL.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 001117, 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 completed its review and has no objection to the use of *N. crassa* fungal protein as a binder in FSIS-regulated meat and poultry products at levels up to 50% of the total product formulation.

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[2] The maximum dose tested in this study was 5,000 mg per kg body weight per day.

[3] BMC discusses two published studies used by other authoritative risk assessment bodies to assert that dietary consumption of < 2 g total nucleic acid from a single-cell protein source per person per day is safe. BMC additionally notes that batch analyses of the fungal protein demonstrate that it meets a specification limit for total RNA of < 2%.

Regarding labeling, meat and poultry products containing the protein are required to be labeled in the ingredients statement with the common or usual name. The common or usual name for this substance is "*Neurospora crassa* mycoprotein." Please contact Ms. Rosalyn Murphy-Jenkins at (301) 504-0878 or via email at Rosalyn.Murphy-Jenkins@usda.gov if you have questions regarding labeling.

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

Conclusions

Based on the information that BMC provided, as well as other information available to FDA, we have no questions at this time regarding BMC's conclusion that fungal protein is GRAS under its intended conditions of use. This letter is not an affirmation that fungal protein 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 001117 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2024.07.09 17:09:43 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety
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cc: Stephanie Hretz, MPH, CPH
Director
Risk Management and Innovations Staff
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