



Nicole K. Berzins
MycoTechnology, Inc.
18250 E. 40th, Ste. 50
Aurora, CO 80011

Re: GRAS Notice No. GRN 000848

Dear Ms. Berzins:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000848. We received MycoTechnology, Inc.'s (MycoTechnology) notice on February 27, 2019 and filed it on May 9, 2019. MycoTechnology submitted an amendment to the notice on July 26, 2019 to provide the strain designation of the *Lentinula edodes* (shiitake) used and the discussion that the putative or potential bioactive constituents of *L. edodes* are not a safety concern under the intended conditions of use.

The subject of the notice is pea and rice protein fermented by shiitake mycelia, for use as a food ingredient, formulation aid, and texturizer in baked goods and baking mixes, beverages and beverage bases, breakfast cereals, dairy product analogs, fats and oils, grain products and pastas, milk products, plant protein products, processed fruits and fruit juices, processed vegetable and vegetable juices, soups and soup mixes,¹ non-baked goods (bars), and confectionary, at levels ranging from 1.0% to 40% of the final food. MycoTechnology also intends to use pea and rice protein fermented by shiitake mycelia in sports nutrition at up to 40 g/serving. The notice informs us of MycoTechnology's view that these uses of pea and rice protein fermented by shiitake mycelia are GRAS through scientific procedures.

MycoTechnology provides information on the identity and composition of pea and rice protein fermented by shiitake mycelia. MycoTechnology describes the ingredient as a tan colored powder comprised of $\geq 75\%$ protein on a dry basis. MycoTechnology states that the pea and rice protein fermented by shiitake mycelia also contains fat, carbohydrates, and 5% solids from the fermentation process (of which $< 0.1\%$ wt/wt is shiitake mycelia biomass).

MycoTechnology provides a description of the multi-stage manufacturing process for pea and rice protein fermented by shiitake mycelia. MycoTechnology states that a starter culture of shiitake mycelia is used to build up a pure shiitake mycelial biomass in the presence of added fermentation media components, including approximately 2% slurry of pea protein and rice protein concentrate, maltodextrin, antifoam agent, and carrot powder. This is followed by a main fermentation step where the built-up biomass

¹ Excluding foods under the jurisdiction of the United States Department of Agriculture.

is combined with sterile pea and rice protein raw materials under controlled conditions. Fermentation is terminated by heat treatment after 20-40 hours, and the resulting protein is concentrated and spray-dried. MycoTechnology states that pea and rice protein fermented by shiitake mycelia is manufactured consistent with current good manufacturing practice with all input materials either approved as food additives or GRAS for their respective uses.

MycoTechnology provides specifications for pea and rice protein fermented by shiitake mycelia. These include protein content ($\geq 75\%$ on a dry basis), aerobic count ($< 10^4$ CFU/g), and limits on moisture ($\leq 7\%$), heavy metals, and microorganisms including *Listeria* (negative in 25 g), *Escherichia coli* (negative in 10 g), *Salmonella* (negative in 25 g). MycoTechnology provides results of analyses from five non-consecutive batches to demonstrate that pea and rice protein fermented by shiitake mycelia can meet the provided specifications. MycoTechnology states that pea and rice protein fermented by shiitake mycelia has a shelf-life of 24 months from the date of manufacture.

MycoTechnology states that pea and rice protein fermented by shiitake mycelia is intended to substitute for, or be used in conjunction with, pea protein, rice protein, and other protein sources in conventional food products. Thus, MycoTechnology states that the intended uses of pea and rice protein fermented by shiitake mycelia will not result in an increase in the overall consumption of protein. MycoTechnology estimates the dietary exposure to pea and rice protein fermented by shiitake mycelia for the total population (consumers only), based on consumption by the U.S. population reported in 2011-2012 National Health and Nutrition Examination Survey Data. MycoTechnology also incorporates estimated dietary exposure data submitted for ingredients described in GRNs 000608 (pea protein concentrate) and 000609 (rice protein concentrate),² and the background dietary exposure to proteins from consumption of peas and rice. MycoTechnology estimates mean and 90th percentile dietary exposure from consumption of pea and rice protein fermented by shiitake mycelia to be 10.3 g/person (p)/d at the mean and 17.3 g/p/d at the 90th percentile, respectively.³ MycoTechnology estimates the maximum dietary exposure to pea and rice protein fermented by shiitake mycelia to be 30.0 g/p/d based on the intended use information provided in GRNs 000608 and 000609. MycoTechnology also estimates the mean and 90th percentile consumption of shiitake mycelia, which is present at $< 0.1\%$ wt/wt in the final food, to be 0.17 mg/kg bw/d and 0.28 mg/kg bw/d respectively.

MycoTechnology discusses publicly available data and information pertinent to the safety of pea and rice protein fermented by shiitake mycelia. First, they discuss relevant information discussed in prior GRNs⁴ (GRN 000581, GRN 000608, and GRN 000788 for pea protein; GRN 000609 for rice protein) to support the general recognition of safety for the starting materials. MycoTechnology states that fermentation with shiitake

² We evaluated GRNs 000608 and 000609 and responded in letters dated May 27, 2016 and June 6, 2016, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

³ FDA calculates these levels at 172 mg/kg bw/d and 288 mg/kg bw/d on a bodyweight basis.

⁴ We evaluated GRNs 000581 and 000788 and responded in letters dated January 25, 2016 and October 12, 2018, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

mycelium is used to alter the organoleptic properties of pea and rice protein concentrates, with little to no alteration to protein composition of the starting raw materials. MycoTechnology states that shiitake mushroom, aside from gill tissue on the undersides of caps producing spores, is composed of compressed mycelia and is compositionally similar to its parent mycelia; they thus conclude safety information for shiitake mushroom, including its safe historical consumption, is directly applicable to shiitake mycelia. MycoTechnology discusses a published 28-day oral gavage toxicity study in Wistar rats in which the study authors concluded that the no-observed-adverse-effect level for aqueous suspension of *L. edodes* mycelia was 2000 mg/kg bw/day. To further corroborate safety, MycoTechnology also discusses other published animal and human studies with *L. edodes* or products derived from *L. edodes*.

MycoTechnology discusses the safety of fungal enzymes in general, including endogenous laccase secreted by shiitake mycelia during manufacturing of their product, which is presumably inactivated during the concentration and spray-drying steps. MycoTechnology also discusses data and information that may negatively impact safety of the product. However, based on the manufacturing processes that involve use of low levels of shiitake mycelia (<0.1 % wt/wt) and heat treatment steps, MycoTechnology concludes it is unlikely that minimum exposure of *L. edodes* from the intended use is a safety concern for the general population.

MycoTechnology includes the statement of a panel of individuals (MycoTechnology's GRAS panel). Based on its review, MycoTechnology's GRAS panel concluded that pea and rice protein fermented by shiitake mycelia is safe under the conditions of its intended use.

Based on the totality of information, MycoTechnology concludes that the intended uses of pea and rice protein fermented by shiitake mycelia are GRAS.

Standards of Identity

In the notice, MycoTechnology states its intention to use pea and rice protein fermented by shiitake mycelia in several food categories, including foods for which standards of identity exist, located in Title 21 of the Code of Federal Regulations. 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.

Potential Labeling Issues

Under section 403(a) of the 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 that contain pea and rice protein fermented by shiitake mycelia 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 Office of Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied

Nutrition. The Office of Food Additive Safety 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.

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 MycoTechnology's notice concluding that pea and rice protein fermented by shiitake mycelia 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 pea and rice protein fermented by shiitake mycelia.

Accordingly, our response should not be construed to be a statement that foods containing pea and rice protein fermented by shiitake mycelia, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).


Conclusions

Based on the information that MycoTechnology provided, as well as other information available to FDA, we have no questions at this time regarding MycoTechnology's conclusion that pea and rice protein fermented by shiitake mycelia is GRAS under its intended conditions of use. This letter is not an affirmation that pea and rice protein fermented by shiitake mycelia 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 000848 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

**Susan J.
Carlson -S**

 Digitally signed by Susan J.
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Susan Carlson, Ph.D.
Director
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