Nathalie Chevreau, Ph.D., R.D.
Chevreau Consulting LLC
2151 E Logan Avenue
Salt Lake City, UT 84108

Re: GRAS Notice No. GRN 001033

Dear Dr. Chevreau:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001033. We received the notice that you submitted on behalf of Fytexia Corp (Fytexia) on November 2, 2021, and filed it on January 31, 2022. Fytexia submitted amendments to the notice on July 21, 2022, September 7, 2022, February 14, 2023, May 10, 2023, and May 16, 2023, providing additional clarifying information about the microorganism, manufacturing process, specifications, dietary exposure assessment, and literature search.

The subject of the notice is hydrolyzed *Saccharomyces cerevisiae* strain ATCC 208288 (yeast hydrolysate) for use as an ingredient in popcorn, chips, and crackers at a level up to 0.83%; meal replacement and snack bars at a level up to 0.63%; and dry protein powders for non-alcoholic beverages at a level up to 1.25%. The notice informs us of Fytexia's view that this use of yeast hydrolysate is GRAS through scientific procedures.

Our use of the term "yeast hydrolysate" 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 nonstandardized foods. Issues associated with labeling and the common or usual name of a food ingredient 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 (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "yeast hydrolysate."

Fytexia describes yeast hydrolysate as a yellow to light brown powder prepared by enzymatic hydrolysis of *S. cerevisiae* strain ATCC 208288. Fytexia states that yeast hydrolysate is composed primarily of protein (50-70%) and carbohydrates (30-40%), with the protein fraction consisting of peptides with molecular weights below 10 kDa.

Fytexia describes the manufacturing process for yeast hydrolysate. A pure culture of *S. cerevisiae* strain ATCC 208288 is grown under controlled conditions. Following fermentation, the yeast suspension is hydrolyzed with a mixture of proteases consisting

of an aminopeptidase, a subtilisin, and a papain. Following hydrolysis, the mixture is heat-treated to inactivate the yeast cells and proteases, and then centrifuged. The supernatant is subjected to membrane filtration and microfiltration, and is then concentrated and heat sterilized. The concentrate is mixed with maltodextrin and spray dried to yield the final yeast hydrolysate. Fytexia states that yeast hydrolysate is manufactured in accordance with current good manufacturing practices

Fytexia provides specifications for yeast hydrolysate that include crude protein content (50-70% (total nitrogen content x 6.25)); carbohydrates (30-40%); ash (≤ 8%); moisture (≤ 8%); lead (≤ 0.2 mg/kg); total aerobic microbial count (≤ 3,000 colony forming units (CFU)/g); total yeasts and mold count (≤ 50 CFU/g); coliforms (absent in 1 g); *Staphylococcus aureus* (absent in 10 g); and *Salmonella* serovars (absent in 20 g). Fytexia provides the results from the analyses of three non-consecutive batches to demonstrate that yeast hydrolysate can be manufactured to meet the specifications. Fytexia states that yeast hydrolysate is stable for at least 36 months at 25 °C and 60% relative humidity and under ambient conditions.

Using food consumption data from the 1999-2016 National Health and Examination Survey (NHANES), Fytexia estimates the eaters-only dietary exposure to yeast hydrolysate from the intended uses to be 0.29 g/person (p)/d at the mean and 0.58 g/p/d at the pseudo-90th percentile[1] for the U.S. population aged 2 years and older.

Fytexia discusses the published safety data and information identified in their literature search to support the safety of yeast hydrolysate. Fytexia states that the *S. cerevisiae* strain is non-pathogenic and non-toxigenic, and that *S. cerevisiae* has a long history of use in food, including uses in bakers yeast extract (21 CFR 184.1983). Fytexia cites Fytexia states that yeast hydrolysate is digested into small peptides and amino acids by pepsin and pancreatic proteases in the stomach and small intestine, respectively, of the consumer. Fytexia discusses published acute oral toxicity and 14-day oral toxicity studies in rats with yeast hydrolysate and concludes that no signs of toxicity were observed during either study. In an amendment dated September 7, 2022, Fytexia discusses a published acute oral toxicity study and 90-day sub-chronic oral toxicity study with yeast hydrolysate in rats. Fytexia states that there were no test article-related adverse effects in either toxicity study.

[1] The pseudo-90th percentile dietary exposure approximates the dietary exposure at the 90th percentile by doubling the mean dietary exposure as described in FDA's "Guidance for Industry: Estimating Dietary Intake of Substances in Food" (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-estimating-dietary-intake-substances-food).

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and 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 yeast hydrolysate 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 Fytexia's notice concluding that yeast hydrolysate 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 yeast hydrolysate. Accordingly, our response should not be construed to be a statement that foods containing yeast hydrolysate, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Fytexia provided, as well as other information available to FDA, we have no questions at this time regarding Fytexia's conclusion that hydrolyzed *S. cerevisiae* ATCC 208288 is GRAS under its intended conditions of use. This letter is not an affirmation that hydrolyzed *S. cerevisiae* ATCC 208288 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 001033 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.05.31 18:16:08 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
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