U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Stella Si
Anchor Center for Certification
No. 1295 Chuan Qiao Road
Building 2, Suite 302
Pudong, Shanghai 201206
CHINA

Re: GRAS Notice No. GRN 001248

Dear Ms. Si:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001248. We received the notice that you submitted on behalf of Shanghai Changing Biotechnology Co., Ltd (Changing Bio) on October 31, 2024, and filed it on April 15, 2025. Changing Bio submitted amendments to the notice on June 20, 2025, August 5, 2025, August 11, 2025, and September 23, 2025, clarifying the production strain, intended uses, manufacturing process, specifications, dietary exposure, and safety narrative.

The subject of the notice is a yeast biomass produced by heat-killed *Kluyveromyces marxianus* CCTCC M 20211265 (HK-*K. marxianus* CCTCC M 20211265) for use as an ingredient and source of protein in the foods and at the maximum use levels as specified in Table 1, excluding uses in infant formula and products under the jurisdiction of the United States Department of Agriculture. The notice informs us of Changing Bio's view that these uses of HK-*K. marxianus* CCTCC M 20211265 are GRAS through scientific procedures.

Table 1. Proposed uses and use levels for HK-*K. marxianus* CCTCC M 20211265

Food category	Food uses	Maximum use level (%)
Baked goods	Bagels, English muffins, cornbread, corn muffins, tortillas	5
	Crackers	5
	Biscuits, cookies	10
	French toast, pancakes, waffles	10
	Bread (high protein)	15
	Tiramisu, trifle, barfi, Puerto Rican style milk dessert	10
	Bean- or meat-filled sweet breads, cheese-, egg-, meat-filled pastries	15

Food category	**Food uses**	**Maximum use level (%)**
Beverages and beverage bases	Special or spiced teas, coffee substitutes, fruit and vegetable flavored gelatin drinks, sport drinks, nutritional drinks and shakes	10
Breakfast cereals	Ready-to-eat, instant, and regular hot cereals	15
Condiments and Relishes	Plain seasoning sauces and spreads, olives, pickles, and relishes, but not spices or herbs	15
Dairy analogs	Non-dairy flavored milk, non-dairy frozen or liquid creamers, non-dairy coffee whiteners, non-dairy toppings, imitation cheese, non-dairy yogurt	8
Frozen dairy desserts	Ice cream, ice milks, sherbets, and other frozen dairy desserts and specialties.	8
Grain products	Noodles, rice noodles, gnocchi	8
Gravies and sauces	Meat sauces and gravies, and tomato, milk, buttery, and specialty sauces.	10
Milk products	Flavored milk and milk drinks, dry milk, yogurt, milk shakes, milk-based smoothies, cream, coffee creamer, whipped toppings, sour cream	8
Meat and egg substitutes	Egg substitutes, bean cakes, meat substitutes	20
Processed fruits	Sorbet, fruit smoothies (with whole fruits, non-dairy, with juice drink, light, bottled), mixed fruit nectar, acai blend fruit juice	9
Snack foods	Chips, pretzels, tortilla chips, popcorn, potato chips and other novelty snacks	15
Candy	Soft candy, including candy bars, chocolates, fudge, mints, and other chewy or nougat candies	5
Soup and soup mixes	Commercially prepared meat, fish, poultry, vegetable, and combination soups and soup mixes (excluding those under the jurisdiction of USDA)	8

Changing Bio discusses the identity of HK-*K. marxianus* CCTCC M 20211265 and describes it as an off-white to light brown powder composed of protein, fiber, moisture, and fat. Changing Bio presents the amino acid profile of the protein component of HK-*K. marxianus* CCTCC M 20211265 and compares it to the profile of other food-derived proteins. Changing Bio states that HK-*K. marxianus* CCTCC M 20211265 was originally isolated from Mongolian cheese (produced using cow's milk) collected from herdsmen in Mongolia, China that is known as "milk tofu." Changing Bio notes that the identity of HK-*K. marxianus* CCTCC M 20211265 was confirmed using internal transcribed spacer sequencing. Changing Bio states that HK-*K. marxianus* CCTCC M 20211265 is non-pathogenic, non-toxigenic, and is deposited in the China Center for Type Culture Collection (CCTCC) under CCTCC M 20211265. Changing Bio states that HK-*K. marxianus* CCTCC M 20211265 is not genetically engineered.

Changing Bio describes the manufacturing process for HK-*K. marxianus* CCTCC M 20211265, stating that it is produced by fermentation in a sterile, contained environment. After fermentation is complete, the fungal biomass is centrifuged to remove the fermentation liquid supernatant. The cell precipitate is then resuspended in water and autoclaved at 105-120°C to inactivate the yeast. The autoclaved cell suspension is then spray dried to produce the final product. Changing Bio states that none of the raw materials used in the manufacturing process are major allergens or are derived from major allergens. Changing Bio states that HK-*K. marxianus* CCTCC M 20211265 is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids are food grade and are approved for their respective uses in accordance with an appropriate U.S. regulation, are GRAS for their intended use, or are the subject of an effective food contact notification.

Changing Bio provides specifications for HK-*K. marxianus* CCTCC M 20211265 that include protein content (≥ 55%), and limits for ash (< 3%), moisture (≤ 7%), total fat content (≤ 6.5%), fiber (≤ 35%), arsenic (≤ 0.1 mg/kg), cadmium (≤ 0.1 mg/kg), mercury ≤ 0.1 mg/kg), lead (≤ 0.1 mg/kg) and microorganisms, including *Salmonella* serovars (negative in 25 g), *Staphylococcus aureus* (<10 CFU/g), and *Escherichia coli* <10 CFU/g). Changing Bio provides the results from the analyses of five non-consecutive batches to demonstrate that HK-*K. marxianus* CCTCC M 20211265 can be manufactured to meet the specifications. Changing Bio states that HK-*K. marxianus* CCTCC M 20211265 has a shelf-life of 12 months at ambient conditions based on results from an accelerated stability study.

Using food consumption data from the 2017-2018 National Health and Examination Survey (NHANES), Changing Bio estimates the eaters-only dietary exposure to HK-*K. marxianus* CCTCC M 20211265 from the proposed uses to be 25 g/p/d at the mean and 53 g/p/d at the 90th percentile for the U.S. population aged 2 years and older. Changing Bio states HK-*K. marxianus* CCTCC M 20211265 is intended to substitute for other proteins in the diet, and thus, the intended uses will not increase the overall consumption of protein. Additionally, Changing Bio states that the 90th percentile dietary exposure to DNA from the intended uses of HK-*K. marxianus* CCTCC M 20211265 will be within the established limit of safe exposure for the U.S. population aged 2 years and older.

Changing Bio presents data and information used to support the safety of HK-*K. marxianus* CCTCC M 20211265. Changing Bio discusses a long history of safe use of the *K. marxianus* species in the human diet, noting its use in fermented dairy products, such as kefir, cheese, and yogurt, and in bread making. Changing Bio states that the European Food Safety Authority (EFSA) includes the species on its Qualified Presumption of Safety (QPS) list. Changing Bio states that *K. marxianus* lacks the biosynthetic pathways required to produce endotoxins or mycotoxins and there is no evidence that it can produce antimicrobial compounds. Changing Bio summarizes the results of studies with other *K. marxianus* species, noting that *K. marxianus* did not demonstrate hemolytic or gelatinase activity. Changing Bio discussed studies examining the cytotoxic potential of *K. marxianus* and its ability to produce pseudohyphae, but states that the risk of pathogenicity is negligible since the manufacturing process includes a heat-inactivation step, ensuring the final product contains no viable yeast cells. Changing Bio conducted a comprehensive literature search to identify all relevant toxicological and clinical studies on *K. marxianus*, noting that the scientific literature reveals a strong safety profile. Changing Bio examined the allergenic potential posed by HK-*K. marxianus* CCTCC M 20211265, discussing a study in which HK-*K. marxianus* CCTCC M 20211265 samples were analyzed via LC-MS/MS. Changing Bio states that all proteins identified by LC-MS/MS were compared to the major allergenic proteins in AllergenOnline databases and other databases and no significant matches were found. This is consistent with the absence of reported cases of allergy in the literature, suggesting that the likelihood of food allergy from HK-*K. marxianus* CCTCC M 20211265 is low.

Based on the totality of the data and information, Changing Bio concludes that HK-*K. marxianus* CCTCC M 20211265 is GRAS for its intended use.

Standards of Identity

In the notice, Changing Bio states its intention to use HK-*K. marxianus* CCTCC M 20211265 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.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and Cosmetic (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 HK-*K. marxianus* CCTCC M 20211265 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 Nutrition Center of Excellence. The Office of Pre-Market 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 Changing Bio's notice concluding that HK-*K. marxianus* CCTCC M 20211265 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 HK-*K. marxianus* CCTCC M 20211265. Accordingly, our response should not be construed to be a statement that foods containing HK-*K. marxianus* CCTCC M 20211265, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Changing Bio provided, as well as other information available to FDA, we have no questions at this time regarding Changing Bio's conclusion that HK-*K. marxianus* CCTCC M 20211265 is GRAS under its intended conditions of use. This letter is not an affirmation that HK-*K. marxianus* CCTCC M 20211265 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 001248 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
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Director
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