U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

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

Re: GRAS Notice No. GRN 001279

Dear Ms. Si:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001279. We received the notice that you submitted on behalf of Angel Yeast Co., Ltd. (Angel Yeast) on May 16, 2025, and filed it on September 22, 2025. Angel Yeast submitted amendments to the notice on January 19, 2026, and February 3, 2026, containing additional information on the intended use, production organism, specifications, dietary exposure, and safety narrative.

The subject of the notice is *Saccharomyces cerevisiae* CCTCC M2025194 for use as a starter culture in distilled spirits fermentation at levels up to 0.5 x 10^9 cells/g of mash. The notice informs us of Angel Yeast's view that this use of *S. cerevisiae* CCTCC M2025194 is GRAS through scientific procedures.

Angel Yeast describes the ingredient as light brown to brown granules. Angel Yeast discusses the identity and construction of *S. cerevisiae* CCTCC M2025194. Angel Yeast states that *S. cerevisiae* CCTCC M2025194 was constructed from *S. cerevisiae* M strain, which was originally isolated from a brewing facility and has a long history of safe use in food applications. *S. cerevisiae* CCTCC M2025194 was constructed using the Obligate Mobile Element Guided Activity (OMEGA) system to insert two glucoamylase (GA) gene cassettes into the host strain. Angel Yeast states that this modification allows the strain to overexpress GA, which is an enzyme that hydrolyzes starch and dextrin into glucose. Angel Yeast states that three plasmids were used to aid in the proper insertion of the expression cassettes into the *S. cerevisiae* M genome. Angel Yeast discusses the results of genotypic and phenotypic analyses and concludes that *S. cerevisiae* CCTCC M2025194 contains the insertion of the two expression cassettes containing the GA coding sequence but does not contain the antibiotic resistance genes used for selection during strain development. Angel Yeast states that the production strain is non-pathogenic and non-toxigenic, and that the strain's identity was confirmed using polymerase chain reaction (PCR), morphological identification, and physiological-biochemical identification. Angel Yeast states that *S. cerevisiae* CCTCC M2025194 is

deposited in the China Center for Type Culture Collection (CCTCC) with the depository number CTCC M2025194.

Angel Yeast states that *S. cerevisiae* CCTCC M2025194 is produced by fermentation in a contained, sterile environment. After fermentation is complete, the fermentation broth is centrifuged to remove the liquid supernatant and concentrate the cell precipitate. The *S. cerevisiae* CCTCC M2025194 cell precipitate is then physically extruded using an extrusion granulator, dried, and broken into granules yielding the final product. Angel Yeast states that *S. cerevisiae* CCTCC M2025194 is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids used in the manufacturing process are food-grade and are used in accordance with applicable U.S. regulations, are GRAS for their intended use, or are the subject of an effective food contact notification. Angel Yeast states that none of the materials used in the manufacture of *S. cerevisiae* CCTCC M2025194 are derived from major food allergens.

Angel Yeast provides specifications for *S. cerevisiae* CCTCC M2025194 that include living cell rate (≥ 80%) and limits for moisture (≤ 7%), ash (≤ 8%), heavy metals, including lead (≤ 0.3 mg/kg), and microorganisms, including coliforms (≤ 10 colony forming units (CFU)/g), *Salmonella* spp. (not detected in 25 g), and *Staphylococcus aureus* (not detected in 25 g). Angel Yeast provides the results from the analyses of five non-consecutive batches to demonstrate that *S. cerevisiae* CCTCC M2025194 can be manufactured to meet these specifications. Angel Yeast states that based on stability studies, *S. cerevisiae* CCTCC M2025194 is stable for 24 months at 25 ± 2 °C and 60 ± 5% relative humidity.

Angel Yeast indicates that the dietary exposure to *S. cerevisiae* CCTCC M2025194 is negligible because the distillation process in the production of distilled spirits effectively removes all yeast cells from the final distilled spirit, and the high alcohol concentration in distilled spirits prevents any yeast survival. Therefore, Angel Yeast concludes that the cumulative dietary exposure to *S. cerevisiae* will not increase due to the intended use of *S. cerevisiae* CCTCC M2025194.

Angel Yeast discusses publicly available data and information to characterize the safety of *S. cerevisiae* CCTCC M2025194. Angel Yeast describes the history of safe use of *S. cerevisiae* species in food and beverage production. Angel Yeast discusses the results of unpublished toxicity studies to evaluate the safety of *S. cerevisiae* CCTCC M2025194 and states that no adverse effects were observed. Angel Yeast describes the GA gene, which was synthesized and derived from *Saccharomycopsis fibuligera*, noting that the gene has a history of safe use in traditional Asian alcoholic fermentation. Angel Yeast discusses the results of *in silico* analyses used to assess the GA gene's allergenic potential. While the results showed a high degree of similarity between the GA gene and a known fungal allergen associated with *Schizophyllum commune*, Angel Yeast explains that the GA gene is only expressed during the fermentation phase of distilled spirits production, and yeast cells containing the GA gene are separated from the final distilled spirits product during the subsequent distillation phase of production. Angel Yeast states that the genetic modifications do not introduce any sequences that would result in

the expression of toxic substances, virulence factors, or other undesirable compounds.

Based on the totality of the data and information, Angel Yeast concludes that *S. cerevisiae* CCTCC M2025194 is GRAS under the conditions of 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 Angel Yeast's notice concluding that *S. cerevisiae* CCTCC M2025194 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 *S. cerevisiae* CCTCC M2025194. Accordingly, our response should not be construed to be a statement that foods containing *S. cerevisiae* CCTCC M2025194, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Angel Yeast provided, as well as other information available to FDA, we have no questions at this time regarding Angel Yeast's conclusion that *S. cerevisiae* CCTCC M2025194 is GRAS under its intended conditions of use. This letter is not an affirmation that *S. cerevisiae* CCTCC M2025194 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 001279 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2026.03.23 10:38:04 -04'00'

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