U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Charles Denby, Ph.D.
Berkeley Fermentation Science Inc.
15555 E 14th Street
Suite 525
San Leandro, CA 94578

Re: GRAS Notice No. GRN 001316

Dear Dr. Denby:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001316. We received Berkeley Fermentation Science Inc. (Berkeley)'s GRAS notice on November 21, 2025, and filed it on April 14, 2026. Berkeley submitted an amendment to the notice on June 30, 2026, providing additional information on the identity of the parent strain and an updated literature search.

The subject of the notice is *Saccharomyces cerevisiae* "BY-1574" (*S. cerevisiae* "BY-1574") for use in brewing to produce non-alcoholic beer (<0.5% alcohol by volume (ABV)) at a level of 1.50×10^6 cells per mL per degree Plato of wort. The notice informs us of Berkeley's view that this use of *S. cerevisiae* "BY-1574" is GRAS through scientific procedures.

Berkeley describes *S. cerevisiae* "BY-1574" as a concentrated liquid slurry of the yeast strain. Berkeley discusses the identity and construction of *S. cerevisiae* "BY-1574" and states that *S. cerevisiae* "BY-1574" is non-pathogenic and non-toxigenic. Berkeley states that *S. cerevisiae* "BY-1574" was constructed from a strain of *S. cerevisiae* called Chico Ale Yeast ("CAY"), an industrial brewing strain with a long history of use in commercial beer production. Berkeley describes the genetic modification as the integration of a synthesized gene encoding an alcohol-O-acyltransferase (AAT) enzyme from *Cucumis melo* var. *Cantalupensis* (*C. melo* var. *Cantalupensis*), regulated by promoter and terminator sequences derived from *S. cerevisiae* strains "CAY" and "S288C", respectively, which are integrated into the genome of the parent strain *S. cerevisiae* strain "CAY" at a single locus, as well as deletion of maltose and maltotriose transporter genes. Berkeley states that successful integration was confirmed by diagnostic polymerase chain reaction and sequencing. Berkeley states that an antibiotic resistance gene used for selection during strain development was subsequently removed from *S. cerevisiae* "BY-1574". During fermentation using *S. cerevisiae* "BY-1574", expression of AAT enzyme catalyzes the production of acetate esters (ethyl acetate, isoamyl acetate, and 2-phenylethyl acetate) imparting fruity, beer-like aromas, while the deletions make the strain unable to consume maltose and maltotriose allowing for arrested fermentation required to produce non-alcoholic beer (< 0.5% ABV).

Berkeley states that *S. cerevisiae* "BY-1574" is manufactured by fermentation of a pure culture under controlled conditions. After fermentation, the temperature is lowered, and the yeast cell mass is separated from the fermentation medium by flocculation and settling. The yeast cell mass is collected as a concentrated liquid slurry. Berkeley states that *S. cerevisiae* "BY-1574" is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids are food-grade, are used in accordance with applicable U.S. regulations, are GRAS for the intended use, or are the subject of an effective food contact notification. Berkeley states that none of the materials used in the manufacture of *S. cerevisiae* "BY-1574" is or is derived from a major food allergen.

Berkeley provides specifications for *S. cerevisiae* "BY-1574" that include viable yeast cells (> 95%) and limits for lead (< 0.01 mg/kg) and microorganisms, including total bacterial count (< 1 per 1×10^6 yeast cells) and total wild yeast (<1 per 1×10^6 yeast cells). Berkeley provides the results from the analyses of three non-consecutive batches to demonstrate that *S. cerevisiae* "BY-1574" can be manufactured to meet these specifications.

Berkeley states that the dietary exposure to *S. cerevisiae* "BY-1574" from the intended uses will be extremely limited because the yeast is removed from beer as part of the standard brewing process. Berkeley states that the intended use of *S. cerevisiae* "BY-1574" is substitutional for other *S. cerevisiae* strains currently used in arrested fermentation for non-alcoholic beer production and, therefore, dietary exposure to *S. cerevisiae* is not expected to increase. Berkeley reports the levels of the flavoring compounds (ethyl acetate, isoamyl acetate, and 2-phenylethyl acetate), maltose, and maltotriose present in beer produced by *S. cerevisiae* "BY-1574" and states that these levels are similar to or less than the levels in commercial beers currently consumed. Therefore, there will be no change in the dietary exposure to these compounds from the intended uses of *S. cerevisiae* "BY-1574".

Berkeley discusses the safety of *S. cerevisiae* "BY-1574" by addressing the safe use of the *S. cerevisiae* parent strain and donor organisms (*S. cerevisiae* "CAY," *S. cerevisiae* strain "S288C" and *C. melo* var. *Cantalupensis*, respectively) and the AAT enzyme in the food industry. Berkeley incorporates into their notice and provides summaries of the data and information pertaining to the safety of genetically engineered *S. cerevisiae* strains used in fermented beverages discussed in GRNs 000120, 000350, 000798, 000841, 001062, 001094, 001096, 001190 and 001252[1]. Berkeley evaluated the AAT enzyme for toxigenic and allergenic potential using bioinformatic analyses and concluded it does not pose a safety concern. Furthermore, untargeted metabolomic analyses did not identify any unexpected metabolic products that would warrant further safety assessment.

[1] Various *S. cerevisiae* strains were the subjects of GRNs 000120, 000350, 000798, 000841, 001062, 001094, 001096, and 001252. We evaluated these notices and responded in letters dated June 30, 2003, February 4, 2011, August 13, 2019, March 10, 2020, April 5, 2023, November 28, 2023, July 5, 2023, and September 23, 2025, respectively, stating that we had no questions at the time regarding the notifiers' GRAS conclusions.

Based on the totality of the data and information, Berkeley concludes that *S. cerevisiae* "BY-1574" is GRAS for 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 Berkeley's notice concluding that *S. cerevisiae* "BY-1574" 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* "BY-1574". Accordingly, our response should not be construed to be a statement that foods containing *S. cerevisiae* "BY-1574", if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Berkeley provided, as well as other information available to FDA, we have no questions at this time regarding Berkeley's conclusion that *S. cerevisiae* "BY-1574" is GRAS under its intended conditions of use. This letter is not an affirmation that *S. cerevisiae* "BY-1574" 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 001316 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

SUSAN J. CARLSON -S

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