U.S. FOOD & DRUG ADMINISTRATION
Human Foods Program

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

Re: GRAS Notice No. GRN 001252

Dear Dr. Denby:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001252. We received Berkeley Fermentation Science Inc. (Berkeley Fermentation Science)'s notice on January 27, 2025, and filed it on April 17, 2025. Berkeley Fermentation Science submitted amendments to the notice on June 27, 2025, and July 30, 2025, providing clarifying information on the analytical methods, manufacturing process, and estimated dietary exposure.

The subject of the notice is *Saccharomyces cerevisiae* "BY-1568" for use as a starter culture at a level of approximately 9 x 10^6 cells/mL of wort in the production of non-alcoholic beer. The notice informs us of Berkeley Fermentation Science's view that this use of *S. cerevisiae* "BY-1568" is GRAS through scientific procedures.

Berkeley Fermentation Science describes *S. cerevisiae* "BY-1568"as a liquid slurry of the yeast strain. Berkeley Fermentation Science states that *S. cerevisiae* "BY-1568"is a non-pathogenic and non-toxigenic yeast. Berkeley Fermentation Science describes the construction of the strain as targeted integration of expression cassettes carrying genes encoding the enzymatic domain of a 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase and a farnesyl pyrophosphate (FPP) synthase with reduced functionality from yeast (*S. cerevisiae*), a linalool synthase from mint (*Mentha citrata*), a geraniol synthase from basil (*Ocimum basilicum),* and an alcohol-O-acyltransferase from cantaloupe (*Cucumis melo* var. *Cantalupenis*), under the control of regulatory elements from *S. cerevisiae*,[1] as well as deletion of four genes related to maltose and maltotriose fermentation. Berkeley Fermentation Science states that the sequence integrity of the insertions was confirmed by polymerase chain reaction (PCR) and DNA sequencing. During beer brewing using *S. cerevisiae* "BY-1568," expression of the introduced genes results in production of flavoring compounds (terpenes and acetate esters) and the gene deletions result in the strain's inability to consume maltose and maltotriose and ferment them to ethanol.

[1] The subject of GRN 000798 is *S. cerevisiae* "yBBS002," a yeast strain for beer brewing, which had HMG-CoA, FPP, linalool synthase, and geraniol synthase genes introduced. We evaluated this notice and responded in a letter dated August 13, 2019, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

Berkeley Fermentation Science describes the manufacture of *S. cerevisiae* "BY-1568" by fermentation of a pure culture under controlled conditions. After fermentation, the culture is cooled, and the yeast cells are separated from the fermentation medium by flocculation and settling. The yeast cell mass is collected as a concentrated liquid slurry. Berkeley Fermentation Science states that *S. cerevisiae* "BY-1568" is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids are food grade and used in accordance with applicable U.S. regulations, are GRAS for their intended use, or are the subject of an effective food contact notification. Berkeley Fermentation Science also states that none of the components used in the manufacturing process include or are derived from any of the major food allergens.

Berkeley Fermentation Science provides specifications for *S. cerevisiae* "BY-1568" that include viable yeast cells (> 95%), limits for lead (≤ 0.01 mg/kg) and microorganisms, including total bacteria (absent per 1 x 10^6 yeast cells) and total wild yeast (absent per 1 x 10^6 yeast cells). Berkeley Fermentation Science provides the results from the analyses of four non-consecutive batches to demonstrate that the ingredient can be manufactured to meet the specifications.

Berkeley states that the intended use of *S. cerevisiae* "BY-1568" is substitutional for the use of other *S. cerevisiae* strains currently used in commercial beer brewing and therefore, the dietary exposure to *S. cerevisiae* is not expected to increase. Berkeley states that *S. cerevisiae* "BY-1568" is removed from beer as part of the standard brewing process, therefore, *S. cerevisiae* "BY-1568" is not expected to be present in the finished beer and the dietary exposure to *S. cerevisiae* "BY-1568" is negligible. Berkeley reports that levels of flavoring compounds (linalool, geraniol, citronellol, ethyl acetate, isoamyl acetate, and 2-phenylethyl acetate) present in beer produced by *S. cerevisiae* "B-1568" are lower than the levels in other commercial beers and therefore, the dietary exposure to these flavoring compounds is not expected to increase from the intended uses of *S. cerevisiae* "B-1568."

Berkeley Fermentation Science uses publicly available data and information to support the safety of *S. cerevisiae* "BY-1568." Berkeley Fermentation Science states that *S. cerevisiae* has a long history of safe use in food. Berkeley Fermentation Science states that the genes introduced into *S. cerevisiae* "BY-1568" do not code for toxic or allergenic proteins, nor are their enzymatic activities implicated in the formation of unanticipated compounds during beer brewing. Berkeley Fermentation Science has determined that there is no safety concern regarding dietary exposure to the flavoring compounds produced during beer brewing with *S. cerevisiae* "BY-1568." Berkley Fermentation Science cites and discusses the results ofthe Food and Agriculture Organization/World Health Organization (FAO/WHO) review of the flavoring compounds to support its conclusion.

Based on the totality of the data and information, Berkeley Fermentation Science concludes that *S. cerevisiae* "BY-1568"is GRAS for its intended use.

Section 301(ll) of the Federal Food, Drug, & Cosmetic (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 Fermentation Science's notice concluding that *S. cerevisiae* "BY-1568" 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-1568." Accordingly, our response should not be construed to be a statement that foods containing *S. cerevisiae* "BY-1568," if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Berkeley Fermentation Science provided, as well as other information available to FDA, we have no questions at this time regarding Berkeley Fermentation Science's conclusion that *S. cerevisiae* "BY-1568" is GRAS under its intended conditions of use. This letter is not an affirmation that *S. cerevisiae* "BY-1568" 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 001252 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2025.09.23 11:14:19 -04'00'

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Director
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