Lance Shaner, Ph.D.
Omega Yeast Labs, LLC
4720 W Pensacola Ave
Chicago, IL 60641

Re: GRAS Notice No. GRN 001190

Dear Dr. Shaner:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001190. We received Omega Yeast Labs, LLC (Omega)'s GRAS notice on February 16, 2024, and filed it on July 1, 2024. Omega submitted an amendment to the notice on September 3, 2024, that clarified the identity, manufacturing process, intended use, dietary exposure, and safety information.

The subject of the notice is *Saccharomyces cerevisiae* "OYR-481" expressing an *aldB* gene encoding acetolactate decarboxylase (AldB) from *Brevibacillus brevis* (*S. cerevisiae* "OYR-481") for use as a starter culture at a level of approximately 1 x 10^6 cells/mL of wort per degree Plato in the production of beer to enhance the flavor profile.[1,2] The notice informs us of Omega's view that this use of *S. cerevisiae* "OYR-481" is generally recognized as safe (GRAS) through scientific procedures.

Omega describes the ingredient as a liquid slurry. Omega discusses the identity and construction of *S. cerevisiae* "OYR-481" and states that *S. cerevisiae* "OYR-481" is non-pathogenic and non-toxigenic. Omega states that *S. cerevisiae* "OYR-481" was constructed by using CRISPR/Cas9 genome editing on the host strain *S. cerevisiae* "OYL-004" originating from the BRY-96 "Beer Pitching Strain," and that *S. cerevisiae* "OYL-004" is widely used in commercial beer production of American craft style beer. Omega describes that the genetic modification is the targeted insertion of a synthesized *B. brevis aldB* gene at the *ADE2* locus on the *S. cerevisiae* "OYL-004" genome. The successful gene editing was confirmed by colony morphology, polymer chain reaction (PCR) and sequencing. Omega states that *S. cerevisiae* "OYR-481" exhibits genotypic and phenotypic characteristics consistent with *S. cerevisiae* "OYL-004" and does not contain the antibiotic resistance gene used for selection during strain development. The *aldB* gene present in *S. cerevisiae* "OYR-481" does not encode any toxic or undesirable protein products.

---

[1] Degrees Plato is used in the brewing industry to quantify the concentration of extract (mainly fermentable sugars but also other soluble solids) in wort as a percentage of weight.
[2] Omega states that the intended use level is consistent with standard brewing industry practice.

Omega states that the manufacture of *S. cerevisiae* "OYR-481" is identical to that of liquid yeast currently used in brewing. *S. cerevisiae* "OYR-481" is produced by aerobic fermentation of a pure culture under controlled, sterile conditions. After fermentation is complete, the culture is cooled and the *S. cerevisiae* "OYR-481" cells are separated from the fermentation medium through flocculation and settling. The remaining yeast cell mass is resuspended to yield a final liquid yeast slurry. Omega states that all raw materials are food-grade and free of the nine major food allergens. Omega further notes that all processing aids are also food-grade, are concluded to be GRAS for their respective uses, and are used in accordance with current good manufacturing practices.

Omega provides specifications for *S. cerevisiae* "OYR-481" that include yeast solids (> 3%), total viable cells (> 98%), and limits for lead (≤ 0.005 mg/kg), total bacteria[3] (< 1 per 2 x 10^6 yeast cells), total wild yeast[4] (< 1 per 2 x 10^6 yeast cells), and *Enterobacteriaceae* (< 10 colony forming units/g). Omega provides the results from the analyses of three non-consecutive batches to demonstrate that *S. cerevisiae* "OYR-481" can be manufactured to meet the specifications.

Omega estimates dietary exposure to *S. cerevisiae* "OYR-481" from the intended uses to be 16.1 x 10^6 cells/kg body weight (bw)/d for men and 14.3 x 10^6 cells/kg bw/d for women for the U.S. population aged 21 years and older, based on the daily consumption for high consumers of beer and the maximum level of *S. cerevisiae* "OYR-481" in the finished beer of 1 x 10^6 cells/mL. Omega states that the intended use of *S. cerevisiae* "OYR-481" 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. Omega notes that *S. cerevisiae* "OYR-481" rapidly declines in viability at the end of beer-brewing fermentation, efficiently flocculates and is discarded after fermentation is completed.

Omega explains the safety of *S. cerevisiae* "OYR-481" by discussing safe use of *S. cerevisiae* species in the food industry, safety of the host strain *S. cerevisiae* "OYL-004" and the AldB enzyme in beer production. Omega incorporates into their notice and provides summaries of the information pertaining to the safety of genetically engineered *S. cerevisiae* strains used in fermented beverages discussed in GRNs 000120, 000175, 000350, 000798, 000841, 001062 and 001096.[5] Omega states that beer fermented with *S. cerevisiae* "OYR-481" will contain comparable levels of alcohol and flavor metabolites as that with the host strain *S. cerevisiae* "OYL-004," with reduced levels of diacetyl.

Based on the totality of the data and information, Omega concludes that *S. cerevisiae* "OYR-481" is GRAS for its intended use.

---

[3] Omega states that "total bacteria" refers to lactic acid bacteria, acetic acid bacteria, and other wort- and beer-spoiling bacteria.
[4] Omega states that "wild yeast" refers to yeasts not normally used in brewing or spoilage organisms, such as *Brettanomyces* spp. and non-*Saccharomyces* spp.
[5] Various *S. cerevisiae* strains were the subjects of GRNs 000120, 000175, 000350, 000798, 000841, 001062 and 001096, respectively. We evaluated these notices and responded in letters dated June 30, 2003, January 6, 2006, February 4, 2011, August 13, 2019, March 10, 2020, April 5, 2023 and July 5, 2023, respectively, stating that we had no questions at the time regarding the notifiers' GRAS conclusions.

Section 301(ll) of the Federal Food, Drug & 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 Omega's notice concluding that *S. cerevisiae* "OYR-481" 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* "OYR-481". Accordingly, our response should not be construed to be a statement that foods containing *S. cerevisiae* "OYR-481", if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Omega provided, as well as other information available to FDA, we have no questions at this time regarding Omega's conclusion that *S. cerevisiae* "OYR-481" is GRAS under its intended conditions of use. This letter is not an affirmation that *S. cerevisiae* "OYR-481" 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 001190 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2024.09.27 14:13:07 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition