

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

Re. GRAS Notice No. GRN 001222

Dear Dr. Shaner:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001222. We received Omega Yeast Labs, LLC (Omega)'s GRAS notice on October 10, 2024, and it on December 23, 2024. Omega submitted an amendment to the notice on February 26, 2025, that clarified the identity and the results from the batch analyses.

The subject of the notice is *Saccharomyces cerevisiae* "OYR-542" (*S. cerevisiae* "OYR-542") for use as a starter culture at a level of approximately 1×10^6 cells/mL of wort per degree Plato in the fermentation of beer to mitigate the formation of yeast-derived haze.^{1,2} The notice informs us of Omega's view that this use of *S. cerevisiae* "OYR-542" is generally recognized as safe (GRAS) through scientific procedures.

Omega describes *S. cerevisiae* "OYR-542" as a liquid slurry. Omega discusses the identity and construction of *S. cerevisiae* "OYR-542" and states that *S. cerevisiae* "OYR-542" is non-pathogenic and non-toxicogenic. Omega states that *S. cerevisiae* "OYR-542" was constructed by using CRISPR/Cas9 gene-editing technology to disrupt the targeted *hzy1* gene and *flo5-hzy1* gene fusion on the host strain *S. cerevisiae* "OYL-011." Omega states that *S. cerevisiae* "OYL-011" is an industrial brewing strain that traces back to a British Brewery in 1971 and has been widely used in commercial beer production of American craft style beer. The successful gene editing was confirmed by colony morphology, polymerase chain reaction (PCR) and sequencing. Omega states that *S. cerevisiae* "OYR-542" exhibits genotypic and phenotypic characteristics consistent with the host strain *S. cerevisiae* "OYL-011" and does not contain the antibiotic resistance gene used for selection during strain development. Omega states that the genetic modification does not generate any toxic or allergenic proteins, or proteins implicated in the formation of undesirable compounds.

Omega states that the manufacture of *S. cerevisiae* "OYR-542" is identical to that of liquid yeast currently used in brewing. *S. cerevisiae* "OYR-542" 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-542" 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 *S. cerevisiae* "OYR-542" is manufactured in accordance with good manufacturing practices and that all raw materials and processing aids are food-grade and are GRAS for their respective uses. Omega states that the raw materials do not contain any major allergens.

Omega provides specifications for *S. cerevisiae* "OYR-542" that include yeast solids (> 3%), total viable cells (> 98%), and limits for lead (≤ 0.005 mg/kg), total bacteria^[3] (< 1 per 2×10^6 yeast cells), total wild yeast^[4] (< 1 per 2×10^6 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-542" can be manufactured to meet the specifications.

Omega estimates the dietary exposure to *S. cerevisiae* "OYR-542" from the intended uses for high consumers of beer to be 16.1×10^6 cells/kg body weight (bw)/d for men and 14.3×10^6 cells/kg bw/d for women for the U.S. population aged 21 years and older, based on the daily consumption of beer and the maximum level of *S. cerevisiae* "OYR-542" in the finished beer of 1×10^6 cells/mL. Omega states that the intended use of *S. cerevisiae* "OYR-542" 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-542" 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-542" by discussing the safe use of *S. cerevisiae* species in the food industry and the safety of the host strain *S. cerevisiae* "OYL-011". 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, 001096, and 001190.^[5] Omega states that beer fermented with *S. cerevisiae* "OYR-542" will contain comparable levels of alcohol and flavor metabolites as that fermented with the host strain *S. cerevisiae* "OYL-011," with reduced levels of haze.

Based on the totality of the data and information, Omega concludes that *S. cerevisiae* "OYR-542" 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 Omega's notice concluding that *S. cerevisiae* "OYR-542" 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-542”. Accordingly, our response should not be construed to be a statement that foods containing *S. cerevisiae* “OYR-542”, 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-542” is GRAS under its intended conditions of use. This letter is not an affirmation that *S. cerevisiae* “OYR-542” 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 001222 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,
**Susan J.
Carlson -S**

 Digitally signed by Susan J.
Carlson -S
Date: 2025.05.05 17:03:38
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Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
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Supplements, and Innovation
Human Foods Program

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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.
 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, 001096 and 001190, 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, July 5, 2023 and September 27, 2024 respectively, stating that we had no questions at the time regarding the notifiers’ GRAS conclusions.