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

Re: GRAS Notice No. GRN 001062

Dear Dr. Shaner:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001062. We received Omega Yeast Labs, LLC's (Omega) notice on March 4, 2022, and filed it on July 19, 2022. Omega submitted amendments to the notice on October 27, 2022, and December 21, 2022, containing additional information regarding the production organism, manufacturing method, analytical methods, specifications, intended use, dietary exposure, and safety of the ingredient.

The subject of the notice is *Saccharomyces cerevisiae* strain "OYR-185" (*S. cerevisiae* "OYR-185") for use as a starter culture at a level of approximately 1 million cells/mL of wort per degree of Plato in the production of beer to enhance the flavor profile of the finished beer.[1,2] The notice informs us of Omega's view that this use of *S. cerevisiae* "OYR-185" is GRAS through scientific procedures.

Omega describes the ingredient as a liquid slurry. Omega discusses the identity and construction of *S. cerevisiae* "OYR-185" and states that *S. cerevisiae* "OYR-185" is non-pathogenic and non-toxigenic, and that the strain's identity was confirmed using Internal Transcribed Spacer sequencing. Omega states that *S. cerevisiae* "OYR-185" is constructed from *S. cerevisiae* strain "OYL-024," an industrial brewing strain of *S. cerevisiae* that is used in commercial production of Belgian-style beer, using CRISPR-Cas9 to introduce a loss of function mutation into the genome of *S. cerevisiae* strain "OYL-024" at the *FDC1* loci. This results in the expression of a truncated fdc1 protein. Omega states that this mutation eliminates the ability of *S. cerevisiae* "OYR-185" to form 4-vinyl guaiacol and results in the production of beer with little to no phenolic flavor. Omega discusses the results of phenotypic and genotypic characterization and concludes that *S. cerevisiae* "OYR-185" contains the loss of function mutation but does not contain the antibiotic resistance gene used for selection during strain development.

Omega states that the manufacture of *S. cerevisiae* "OYR-185" is identical to that of liquid yeast currently used during brewing. *S. cerevisiae* "OYR-185" is produced by

[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.

aerobic fermentation of a pure culture under controlled conditions. When the fermentation is complete, the *S. cerevisiae* "OYR-185" cells are separated from the fermentation medium through flocculation and settling. The fermentation medium is then decanted, and the remaining yeast cell mass is resuspended to yield a final liquid yeast slurry. Omega states that no components of the fermentation medium are allergens or are derived from allergenic sources, and that *S. cerevisiae* "OYR-185" is manufactured in accordance with current good manufacturing practices using food-grade raw materials.

Omega provides specifications for *S. cerevisiae* "OYR-185" that include percent 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-185" can be manufactured to meet the specifications.

Omega states that the use of *S. cerevisiae* "OYR-185" will be 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 the yeast efficiently flocculates and rapidly declines in viability at the end of alcoholic fermentation. Omega further states that *S. cerevisiae* "OYR-185" is largely removed during the beer clarification processes and therefore only a negligible amount of the non-viable yeast, if any, would be present in the finished beer.

Omega uses publicly available data and information to characterize the safety of *S. cerevisiae* "OYR-185." Omega describes *S. cerevisiae* as a well-characterized production organism with a history of safe use in the food industry. Omega states that the loss of function mutation does not result in the expression of toxic or allergenic proteins and does not code for proteins that form undesirable compounds. Omega discusses the resulting truncated fdc1 protein expressed due to the loss of function mutation and states that this truncated protein is naturally expressed in other industrial brewing strains with no known adverse effects.

Based on the available data and information, Omega concludes that *S. cerevisiae* "OYR-185" 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

[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 spoiling organisms such as *Brettanomyces* spp. and non-*Saccharomyces* spp.

section 301(ll)(1)-(4) applies. In our evaluation of Omega's notice concluding that *S. cerevisiae* "OYR-185" 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-185." Accordingly, our response should not be construed to be a statement that foods containing *S. cerevisiae* "OYR-185," 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-185" is GRAS under its intended conditions of use. This letter is not an affirmation that *S. cerevisiae* "OYR-185" 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 001062 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.04.05 11:02:39 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
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