U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

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

Re: GRAS Notice No. GRN 001251

Dear Dr. Shaner:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001251. We received Omega Yeast Labs, LLC (Omega)'s notice on January 13, 2025, and filed it on April 17, 2025. Omega submitted an amendment to the notice on June 30, 2025, providing clarifying information on a specification and discussion of the cited toxicology studies.

The subject of the notice is *Saccharomyces cerevisiae* "OYR-290" expressing a gene encoding a cysteine-thiol lyase from *Staphylococcus hominis* (*S. cerevisiae* "OYR-290") 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-290" is GRAS through scientific procedures.

Omega describes *S. cerevisiae* "OYR-290" as a liquid slurry of the yeast strain. Omega states that *S. cerevisiae* is a non-pathogenic and non-toxigenic yeast. Omega describes the construction of the strain from *S. cerevisiae* strain "Chico," a brewer's yeast commonly used in commercial beer production, by targeted integration of an expression cassette carrying a gene encoding a cysteine-thiol lyase from *S. hominis* under the control of a promoter and a terminator from *S. cerevisiae*. Omega states that the sequence integrity of the insertion was confirmed by polymerase chain reaction (PCR). During beer fermentation using *S. cerevisiae* "OYR-290", the expressed cysteine-thiol lyase enhances the release of 3- sulfanylhexan-1-ol (3SH), the volatile thiol that imparts tropical fruit flavor to the beer.

Omega describes the manufacture of *S. cerevisiae* "OYR-290" 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, followed by decanting of the medium. The yeast cell mass is resuspended as a concentrated liquid slurry. Omega states that *S. cerevisiae* "OYR-290" is manufactured

[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.

in accordance with current good manufacturing practices and that all raw materials are standard food-grade ingredients used in the manufacturing of liquid brewing yeast. Omega further states that the processing aids are food-grade and are GRAS for their intended use. Omega also states that no components used in the manufacturing process include or are derived from major food allergens.

Omega provides specifications for *S. cerevisiae* "OYR-290" that include yeast solids (> 3%), total viable cells (> 98%), limits for heavy metals, including lead (≤ 0.005 mg/kg) and microorganisms, including 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 (CFU)/g). Omega provides the results from the analyses of three non-consecutive batches to demonstrate that *S. cerevisiae* "OYR-290" can be manufactured to meet the specifications.

Omega estimates the dietary exposures to *S. cerevisiae* "OYR-290" 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 use level of *S. cerevisiae* "OYR-290" in the finished beer of 1 x 10^6 cells/mL. Omega states that the intended use of *S. cerevisiae* "OYR-290" 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-290" rapidly declines in viability at the end of beer brewing, efficiently flocculates, and is discarded once fermentation is completed. Omega reports that beers produced using *S. cerevisiae* "OYR-290" contain up to of 18 µg of 3SH/L. Omega estimates the dietary exposures to 3SH from the intended uses of *S. cerevisiae* "OYR-290" to be 0.29 µg/kg bw/d for men and 0.26 µg/kg bw/d for women for the U.S. population aged 21 years and older.

Omega uses publicly available data and information to support the safety of *S. cerevisiae* "OYR-290." Omega states that *S. cerevisiae* has a history of safe use in the food industry. Omega states that the introduced *S. hominis* gene does not code for toxic or allergenic proteins. Omega indicates that as a result of expression of the cysteine-thiol lyase, beers produced using *S. cerevisiae* "OYR-290" contain 3SH and the level is within the range measured in wine and tropical fruit juices.

Based on the totality of the data and information, Omega concludes that *S. cerevisiae* "OYR-290" 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

[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.

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-290" 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-290." Accordingly, our response should not be construed to be a statement that foods containing *S. cerevisiae* "OYR-290," 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-290" is GRAS under its intended conditions of use. This letter is not an affirmation that *S. cerevisiae* "OYR-290" 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 001251 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 11:12:24 -04'00'

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