



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

Re: GRAS Notice No. GRN 001096

Dear Dr. Shaner:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001096. We received Omega Yeast Labs, LLC's (Omega) notice on June 29, 2022 and filed it on January 24, 2023. Omega submitted an amendment to the notice on April 5, 2023, 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-243" for use as a starter culture at a level of approximately 1 million cells/mL of wort per degree Plato in the fermentation 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-243" is GRAS through scientific procedures.

Omega describes the ingredient as a liquid slurry. Omega discusses the identity and construction of *S. cerevisiae* "OYR-243" and states that *S. cerevisiae* "OYR-243" 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-243" was constructed from *S. cerevisiae* "OYL-011," an industrial brewing strain of *S. cerevisiae* that is widely used in the production of traditional English beer and modern American beer styles. *S. cerevisiae* "OYR-243" was constructed using CRISPR-Cas9 to insert three DNA sequences: *IRC7*, *TDH3* promoter, and a *CYC1* terminator. Omega states that the *TDH3* and *CYC1* sequences aid in transcription and gene expression, and the *IRC7* sequence encodes a β -lyase enzyme. Omega states that the β -lyase enzyme aids in the production of thiol flavor compounds in beer. Omega discusses the results of phenotypic and genotypic analyses and concludes that *S. cerevisiae* "OYR-243" contains the insertion of the *TDH3-IRC7-CYC1* cassette but does not contain the antibiotic resistance gene used for selection during strain development.

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-243” is identical to that of liquid yeast currently used in brewing. *S. cerevisiae* “OYR-243” 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-243” 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 none of the components of the fermentation medium are allergens or are derived from allergens, and that *S. cerevisiae* “OYR-243” is manufactured in accordance with current good manufacturing practices using food-grade materials. Omega further states that all processing aids used in the manufacture of *S. cerevisiae* “OYR-243” are concluded to be GRAS for their respective uses.

Omega provides specifications for *S. cerevisiae* “OYR-243” that include percent yeast solids (> 3%), total viable cells (> 98%), and limits for lead (≤ 0.005 mg/kg), total bacteria³ (< 1 per 2×10^6 yeast cells), total wild yeast⁴ (< 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-243” can be manufactured to meet the specifications.

Omega states that the intended use of *S. cerevisiae* “OYR-243” 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 provides an estimate of dietary exposure to *S. cerevisiae* “OYR-243” for heavy drinkers of beer of 16.1×10^6 cells/kg body weight (bw)/d and 14.3×10^6 cells/kg bw/d for males and females, respectively.⁵ Omega notes that *S. cerevisiae* “OYR-243” efficiently flocculates and rapidly declines in viability at the end of fermentation. Omega states that the finished beer will contain trace levels of yeast due to the clarification process that largely removes the ingredient. Omega further notes that any remaining yeast will have limited viability and metabolic activity in the packaged beer.

Omega explains the safety of *S. cerevisiae* “OYR-243” by discussing the safety of the *S. cerevisiae* species, the safety of the β -lyase enzyme, and the safety of the thiol compounds produced in the beer. Omega states that *S. cerevisiae* itself and food ingredients produced by *S. cerevisiae* are safe for consumption. Omega notes that several genetically modified *S. cerevisiae* strains have been the subject of previous GRNs for use in fermented beverages.⁶ Omega reports that dietary exposure to *S. cerevisiae* “OYR-243” will not differ from the dietary exposure to other industrial yeast used in commercial beer applications. Omega states that the genetic material inserted 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.

⁵ Based on the trace level of commercial *S. cerevisiae* in finished beer of 1 million cells/ml and daily beer consumption of 1420 mL and 1065 mL for males and females, respectively.

⁶ Various *S. cerevisiae* strains are the subjects of GRNs 000120, 000175, 000350, 000798, and 000841. We evaluated these notices and responded in letters dated June 30, 2003, January 6, 2006, February 4, 2011, August 13, 2019, and March 10, 2020, respectively, stating that we had no questions at those times regarding the notifiers’ GRAS conclusions.

S. cerevisiae to produce strain “OYR-243,” including the gene sequence encoding the β -lyase enzyme, is naturally present in industrial brewing strains of *S. cerevisiae* and there is no foreign genetic material in *S. cerevisiae* “OYR-243.” Omega states that beer fermented with *S. cerevisiae* “OYR-243” contains thiol flavors produced by the β -lyase enzyme, but the levels of these flavors are much lower than those present in many other beers on the market that are currently consumed.

Based on the weight of evidence discussed, Omega concludes that *S. cerevisiae* “OYR-243” is GRAS for the intended use.

Section 301(l) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

Section 301(l) 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(l)(1)-(4) applies. In our evaluation of Omega’s notice concluding that *S. cerevisiae* “OYR-243” is GRAS under its intended conditions of use, we did not consider whether section 301(l) or any of its exemptions apply to foods containing *S. cerevisiae* “OYR-243.” Accordingly, our response should not be construed to be a statement that foods containing *S. cerevisiae* “OYR-243,” if introduced or delivered for introduction into interstate commerce, would not violate section 301(l).

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-243” is GRAS under its intended conditions of use. This letter is not an affirmation that *S. cerevisiae* “OYR-243” 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 001096 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J.
Carlson -S

Susan J. Carlson, Ph.D.
Director

Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

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