U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Wing Yu
CIRS GROUP USA INC
4250 Fairfax Drive
Suite 600
Arlington, VA 22203

Re: GRAS Notice No. GRN 001328

Dear Ms. Yu:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001328. We received the notice that you submitted on behalf of Shandong Weiyan Biotechnology Co., Ltd. (Shandong) on February 12, 2026, and filed it on May 13, 2026. Shandong submitted an amendment on August 10, 2026, clarifying the analytical methods and resulting data, composition, stability, dietary exposure, and safety narrative.

The subject of the notice is β-carotene preparation produced by *Yarrowia lipolytica* (*Y. lipolytica*) CGMCC 33926 expressing genes from *Mucor circinelloides* and *Y. lipolytica* (β-carotene preparation) for use as an ingredient in the foods at the maximum use levels as specified in Table 1, excluding infant formula, alcoholic beverages, and products under the jurisdiction of the United States Department of Agriculture. The notice informs us of Shandong's view that these uses of β-carotene preparation are GRAS through scientific procedures.

Table 1. Proposed uses of β-carotene preparation

Food category	Food uses	Maximum use level (mg/kg)
Baked goods and baking mixes	Breads, rolls, and cakes	10
	Cookies, crackers, and salty snacks	10
Beverages and beverage bases	Soft drinks (orange type only)	10
	Meal replacement shakes, mixes, and functional beverages	10
Breakfast cereals	Ready-to-eat cereals	10
Egg products	Egg substitute products	10
Fats and oils	Vegetable oils and salad dressings	25
	Butter and animal fats	25
	Margarine	25
	Mayonnaise	100

Food category	**Food uses**	**Maximum use level (mg/kg)**
Frozen dairy desserts and mixes	Frozen dairy desserts and mixes	10
Gelatins, puddings, and fillings	Gelatin desserts, puddings, and custards	10
Grain products and pasta	Pastas	10
	Rice dishes	10
	Granola bars and cereal bars	10
Gravies and sauces	Meatless bullions and consommé	200
	Meatless gravies and sauces	10
Plant protein products	Meatless meat products (soy-based imitation meat)	10
Processed fruits and fruit juices	Canned mangoes	100
	Processed fruits, juices, juice drinks, and punches	10
Processed vegetables and vegetable juices	Canned green peas	100
	Picked cucumbers	300
	Processed vegetables and juices	10
Soups and soup mixes	Meatless soups and soup mixes	10
Sweet sauces, toppings, and syrups	Sweet sauces, toppings, and syrups	10
Other	Medical foods	180 mg/d

Shandong provides information on the identity and composition of β-carotene preparation and describes it as a dark red to brownish red, crystalline powder containing ≥ 96% total carotenoids. Shandong states that β-carotene is one of the most abundant carotenoids in the human diet and serves as the primary dietary source of vitamin A. Shandong indicates that β-carotene has the molecular formula $C_{40}H_{56}$, molecular weight of 536.88 g/mol, and CAS registry number 7235-40-7. Shandong states that the identity of β-carotene preparation is confirmed using IR, UV, proton and ^{13}C NMR spectroscopy, and high-resolution mass spectrometry.

Shandong describes the production strain used to manufacture β-carotene preparation. Shandong states that *Y. lipolytica* CGMCC 33926 is nonpathogenic and nontoxigenic and is genetically engineered from the taxonomically identified parental strain, *Y. lipolytica* PO1f. Shandong states that the production strain was constructed through integration of four genes (two from *M. circinelloides*, and two from *Y. lipolytica*) for the biosynthesis of β-carotene, two marker genes from *Y. lipolytica* for strain construction, and deletion of an endogenous, enzyme-encoding gene to enhance homologous recombination efficiency, gene targeting, and stable integration. Shandong discusses the results of sequencing analyses demonstrating the stable integration of the genes used to construct the production strain. Shandong states that the production strain is deposited in the China General Microbiological Culture Collection Center under the deposition number CGMCC 33926.

Shandong describes the manufacturing process for β-carotene preparation, which is produced by fermentation of a pure culture of *Y. lipolytica* CGMCC 33926 under controlled conditions. Following fermentation, the yeast cells are concentrated using membrane filtration and lysed by high-pressure homogenization. The lysate is filtered using a plate-and-frame filter press, and the β-carotene is extracted from the lysate using ethyl acetate. The resulting slurry containing β-carotene is concentrated, crystallized, and purified by filtration. The crystals are then vacuum dried and sieved to yield the final product. Shandong states that β-carotene preparation is manufactured in accordance with current good manufacturing practices and that all starting materials and processing aids are food grade and approved for their respective uses in accordance with applicable U.S. regulations, are GRAS for their intended uses, or are the subject of an effective food contact notification. Shandong states that none of the raw materials used during the manufacturing process are, or are derived from, major food allergens.

Shandong provides specifications for β-carotene preparation that include total carotenoids, (96-101% (calculated as β-carotene)), α-carotene (≤ 1%, of total carotenoids), total related compounds including α-carotene (≤ 5% of total carotenoids), loss on drying (≤ 0.2% w/w), ash (≤ 0.2% w/w), ethyl acetate (≤ 0.8% w/w), heavy metals, including lead (≤ 0.1 mg/kg), and microorganisms. Shandong provides the results from the analyses of three non-consecutive batches to demonstrate that β-carotene preparation can be manufactured to meet the specifications. Shandong states that β-carotene preparation is stable for one year when stored in a sealed, light-protective container at room temperature (25°C and 60% relative humidity).

Shandong provides estimates of dietary exposure to β-carotene preparation based on the intended uses and food consumption data from the 2021-2023 National Health and Nutrition Examination Survey. Shandong estimates the eaters-only dietary exposure to β-carotene preparation from the intended uses to be 4.6 mg/p/d at the mean and 8.3 mg/p/d at the 90th percentile for the U.S. population aged 2 years and older. Shandong states that their intended use of β-carotene preparation is identical to that described in GRN 000320[1]; therefore, they do not expect their intended use to increase the dietary exposure to β-carotene. Shandong provides an updated cumulative dietary exposure to β-carotene from the background intake of β-carotene in food combined with the intended uses to be 6.4 mg/p/d at the mean and 11.4 mg/p/d at the 90th percentile for the U.S. population aged 2 years and older.

In support of the safety of consumption of β-carotene preparation, Shandong discusses published acute and subchronic animal toxicity studies; published reproductive, developmental, and genotoxicity studies, and information on the absorption, distribution, metabolism, and excretion of dietary β-carotene. Shandong discusses their conclusion and based on the available data, their intended use of β-carotene preparation raises no safety concerns for the general population. Shandong also notes that the use β-carotene is affirmed as GRAS under 21 CFR 184.1245, and that FDA had no questions in

[1] β-carotene is the subject of GRN 000320. We evaluated this GRAS notice and responded in a letter dated September 3, 2010, stating that we had no questions at that time about the notifier's GRAS conclusion.

response to GRN 000320, which described the use of palm oil carotenoids including β-carotene.

Based on the totality of the data and information, Shandong concludes that β-carotene preparation is GRAS for its intended use.

Standards of Identity

In the notice, Shandong states its intention to use β-carotene preparation in several food categories, including foods for which standards of identity exist, located in Title 21 of the Code of Federal Regulations (CFR). We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, & Cosmetic (FD&C) Act, a food is misbranded if its labeling is false or misleading in any way. Section 403(r) of the FD&C Act lays out the statutory framework for labeling claims characterizing a nutrient level in a food or the relationship of a nutrient to a disease or health-related condition (also referred to as nutrient content claims and health claims). If products containing β-carotene preparation bear any nutrient content or health claims on the label or in labeling, such claims are subject to the applicable requirements and are under the purview of the Office of Nutrition and Food Labeling (ONFL) in the Nutrition Center of Excellence (NCE). The Office of Pre-Market Additive Safety (OPMAS) did not consult with ONFL on this issue or evaluate any information in terms of labeling claims. Questions related to food labeling should be directed to ONFL.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, Shandong describes β-carotene preparation as a dark red to brownish red powder. As such, the use of β-carotene preparation in food products may constitute a color additive use under section 201(t)(1) of the FD&C Act and FDA's implementing regulations in 21 CFR Part 70. Under section 201(t)(1) and 21 CFR 70.3(f), a color additive is a material that is a dye, pigment, or other substance made by a synthetic process or similar artifice, or is extracted, isolated, or otherwise derived from a vegetable, animal, mineral, or other source. Under 21 CFR 70.3(g), a material that otherwise meets the definition of a color additive can be exempt from that definition if it is used (or is intended to be used) solely for a purpose or purposes other than coloring. Our response to GRN 001328 is not an approval for use as a color additive nor is it a finding of the Secretary of the Department of Health and Human Services within the meaning of section 721(b)(4) of the FD&C Act. Questions about color additives should be directed to the Division of Food Ingredients in OPMAS.

Medical Foods

Shandong informed us of its intent to use β-carotene preparation in medical foods. Section 5(b)(3) of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)) defines a medical food as a "food formulated to be consumed or administered enterally under a physician's supervision." This provision also specifies that a medical food is "intended for the specific dietary management of a disease or condition with distinctive nutritional requirements, based on recognized scientific principles, established by a medical evaluation." Medical foods, including how they are labeled, are the purview of the Office of Critical Foods (OCF) in the NCE. The Office of Pre-Market Additive Safety did not consult with OCF about whether any particular food product containing β-carotene preparation as an ingredient would be a medical food. Questions about medical foods should be addressed to OCF.

Section 301(ll) of the 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 Shandong's notice concluding that β-carotene preparation 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 β-carotene preparation. Accordingly, our response should not be construed to be a statement that foods containing β-carotene preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Starlight provided, as well as other information available to FDA, we have no questions at this time regarding Shandong's conclusion that β-carotene preparation is GRAS under its intended conditions of use. This letter is not an affirmation that β-carotene preparation 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 001328 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

SUSAN J. CARLSON -S

Digitally signed by SUSAN J. CARLSON -S
Date: 2026.09.08 09:58:18 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Pre-Market Additive Safety
Office of Food Chemical Safety, Dietary Supplements, and Innovation
Human Foods Program