



Erik Tietig
Miracle Fruit Farm LLC
16300 SW 184th Street
Miami, FL 33187

Re: GRAS Notice No. GRN 001144

Dear Mr. Tietig:

This letter corrects our response letter to GRN 001144 signed on December 20, 2023. The purpose of this revised letter is to correct the name of the substance in the “Conclusions” section of our December 20, 2023 letter.

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001144. We received Miracle Fruit Farm LLC (Miracle Fruit Farm)’s notice on May 9, 2023, and filed it on August 15, 2023. Miracle Fruit Farm submitted an amendment to the notice on November 6, 2023, that provided additional information pertaining to the intended use, manufacturing methods, specifications, results from the batch analyses, and estimates of dietary exposure.

The subject of the notice is miracle fruit (*Synsepalum dulcificum*) powder (miracle fruit powder) for use as a taste modifier¹ at a maximum level of 0.005% in water-based beverages.^{2, 3} The notice informs us of Miracle Fruit Farm’s view that these uses of miracle fruit powder are GRAS through scientific procedures.

Our use of the term, “miracle fruit (*Synsepalum dulcificum*) powder” or “miracle fruit powder,” in this letter is not our recommendation of that term as an appropriate common or usual name for declaring the substance in accordance with FDA’s labeling requirements. Under 21 CFR 101.4, each ingredient must be declared by its common or usual name. In addition, 21 CFR 102.5 outlines general principles to use when establishing common or usual names for nonstandardized foods. Issues associated with labeling and the common or usual name of a food ingredient are under the purview of

¹ Miracle Fruit Farm states that under the intended conditions of use, miracle fruit powder imparts sweetness by modifying taste perception from sour to sweet due to the glycoprotein miraculin. Miracle Fruit Farm reports that the taste-modifying effect of miraculin is rapid with no lasting desensitization effect and no effect on other taste qualities.

² Miracle Fruit Farm states that the intended use in water-based beverages includes products such as sweetened or flavored bottled waters, coconut water, and sugar cane beverage; however, the intended uses exclude soft drinks, sports drinks, and “energy” drinks.

³ Miracle Fruit Farm states that miracle fruit powder is not intended for use in infant formula, infant food products, or in foods that are under the jurisdiction of the United States Department of Agriculture.

the Office of Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety (OFAS) did not consult with ONFL regarding the appropriate common or usual name for “miracle fruit (*Synsepalum dulcificum*) powder” or “miracle fruit powder.”

Miracle Fruit Farm describes miracle fruit powder as the dried and deseeded fruit of *S. dulcificum*. Miracle Fruit Farm states that miracle fruit powder is a red or red-brown to pink colored powder that is composed of carbohydrates, protein, ash, and moisture. Miracle Fruit Farm states that the intended technical effect is attributed to a glycoprotein, miraculin, present in miracle fruit powder. Miracle Fruit Farm states that miraculin has a molecular weight of 24,600 Da and consists of 220 amino acid residues, including a 29 amino acid peptide that is removed through post-translational processing. Miracle Fruit Farm states that miraculin exists as a homodimer and notes that the sequence of miraculin is publicly available (Uniprot Accession No. P13087).

Miracle Fruit Farm describes the method of manufacture for miracle fruit powder and notes that it is manufactured in accordance with current good manufacturing practices (cGMP). Miracle Fruit Farm states that the manufacture of miracle fruit powder involves only physical processing steps and does not use any organic solvents or processing aids. Fresh miracle fruit is harvested, washed, and the seeds are removed. The deseeded fruit is pulped and macerated, and the product is then freeze-dried, milled, and sieved to obtain miracle fruit powder.

Miracle Fruit Farm provides specifications for miracle fruit powder that include miraculin ($\geq 0.048\%$ dry basis (DB)), carbohydrates ($\geq 80\%$ DB), protein ($\geq 4.5\%$ DB), total fatty acids expressed as triglyceride equivalents ($\geq 0.4\%$ DB), and limits for moisture ($< 6\%$), ash ($< 6\%$ DB), arsenic (< 0.1 mg/kg), lead (< 0.1 mg/kg), cadmium (< 0.1 mg/kg), mercury (< 0.1 mg/kg), and microorganisms. Miracle Fruit Farm provides the results from the analyses of nine non-consecutive batches to demonstrate that miracle fruit powder can be manufactured to meet these specifications. Miracle Fruit Farm provides the results of a 52-week stability study of miracle fruit powder stored at 25 °C and 60% relative humidity. Based on the results of that study, Miracle Fruit Farm concludes that miracle fruit powder is stable for up to 52 weeks when stored at ambient temperature and humidity.

Miracle Fruit Farm provides estimates of dietary exposure to miracle fruit powder based on the intended uses and food consumption data from 2015-2016 National Health and Nutrition Examination Survey (NHANES). Miracle Fruit Farm estimates the mean and 90th percentile eaters-only dietary exposure to miracle fruit powder for the U.S. population aged 2 years and older to be 16.5 mg/person (p)/d (253 µg/kg body weight (bw)/d) and 36 mg/p/d (519 µg/kg bw/d), respectively. Miracle Fruit Farms provides estimates of dietary exposure to miraculin based on the intended uses of miracle fruit powder and the highest concentration of miraculin (i.e., 0.32%) found in the analyses of nine, non-consecutive batches. Miracle Fruit Farm reports the mean and 90th percentile eaters-only dietary exposure to miraculin for the U.S. population aged 2 years and older to be 52.8 µg/p/d and 115.2 µg/p/d, respectively.

Miracle Fruit Farm discusses publicly available data and information supporting the safety of miracle fruit powder and miraculin protein. Miracle Fruit Farms notes that miracle fruit powder is substantially equivalent to its source, miracle fruit from the *S. dulcificum* plant. Miracle fruit powder is primarily composed of macronutrients, including carbohydrates and fiber, and polyphenolic compounds that are common components of human food. Miracle Fruit Farm states that the safety of the intended use of miracle fruit powder and miraculin is supported by the previous human consumption of *S. dulcificum* fruit as a component of the diet in endemic regions of Africa, and subsequent cultivation and consumption in the United States. Miracle Fruit Farm estimates that the highest (90th percentile) dietary exposure to miracle fruit powder would be equivalent to consumption of approximately 40% of a single miracle fruit. Miracle Fruit Farm details the biochemical mechanism of miraculin effects on sweet taste receptors.

Miracle Fruit Farm summarizes the results of a comprehensive literature search to identify available safety information relevant to miracle fruit powder and miraculin. Miracle Fruit Farm does not identify any safety concerns or information that would contradict its GRAS conclusion. Miracle Fruit Farm corroborates the safety of miracle fruit powder utilizing the results of unpublished genotoxicity and toxicity studies conducted with dried miracle fruit test materials. Miracle Fruit Farm also summarizes published and unpublished human studies evaluating the taste-modifying effect of miracle fruit and miracle fruit powder. Miracle Fruit Farm concludes that miracle fruit preparations were well tolerated and that the intended use of miracle fruit powder is unlikely to result in prolonged effects on taste perception.

Based on the weight-of-evidence, including results of *in silico* and *in vitro* digestibility assessments, and published *in silico* sequence alignment-based approaches, Miracle Fruit Farm concludes that miraculin does not pose an allergenic or toxigenic risk to consumers.

Based on the totality of information, Miracle Fruit Farm concludes that miracle fruit powder is GRAS for its intended use.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, Miracle Fruit Farm describes miracle fruit powder as a red or red-brown to pink colored powder. As such, the use of miracle fruit powder in food products may constitute a color additive use under section 201(t)(1) of the Federal Food, Drug, and Cosmetic Act (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 001144 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 OFAS.

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 Miracle Fruit Farm’s notice concluding that miracle fruit powder 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 miracle fruit powder. Accordingly, our response should not be construed to be a statement that foods containing miracle fruit powder, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Miracle Fruit Farm provided, as well as other information available to FDA, we have no questions at this time regarding Miracle Fruit Farm’s conclusion that miracle fruit powder is GRAS under its intended conditions of use. In 1977, FDA determined that miracle fruit (*S. dulcificum*) berries, concentrates, and extracts are unapproved food additives (42 FR 26467, May 24, 1977); however, based on our review of the data and information provided in GRN 001144 and the state of current scientific knowledge, the 1977 determination does not apply to the subject of this notice under the intended conditions of use. This letter is not an affirmation that miracle fruit powder 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 001144 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson

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Susan J. Carlson, Ph.D.

Director

Division of Food Ingredients

Office of Food Additive Safety

Center for Food Safety

and Applied Nutrition