



Susan Cho, Ph.D.
NutraSource, Inc.
6309 Morning Dew Court
Clarksville, MD 21029

Re: GRAS Notice No. GRN 000784

Dear Dr. Cho:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000784. We received the notice that you submitted on behalf of Hunan Huacheng Biotech, Inc. (Hunan Huacheng) on May 18, 2018, and filed it on June 25, 2018. Hunan Huacheng submitted an amendment to the notice on November 5, 2018, including a statement regarding the results of one of the studies described in the notice.

The subject of the notice is *Siraitia grosvenorii* Swingle (Luo Han Guo) fruit juice concentrate (containing $\geq 0.6\%$, $\geq 2.4\%$, $\geq 3.1\%$, or $\geq 3.9\%$ mogroside V) (SGFJC) for use as a general purpose sweetener in conventional foods, including infant and toddler foods, at levels determined by current good manufacturing practices,¹ and as a table top sweetener. The notice informs us of Hunan Huacheng's view that these uses of SGFJC are GRAS through scientific procedures.

Our use of the term "*Siraitia grosvenorii* Swingle (Luo Han Guo) fruit juice concentrate" or "SGFJC" 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 the Office of Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety did not consult with ONFL regarding the appropriate common or usual name for "*Siraitia grosvenorii* Swingle (Luo Han Guo) fruit juice concentrate" or "SGFJC."

Hunan Huacheng provides information about the identity and composition of SGFJC. Hunan Huacheng describes SGFJC as a mixture of compounds extracted from the fruit of *S. grosvenorii* Swingle, commonly known as Luo Han Guo or monk fruit. The components of SGFJC that are responsible for imparting the characteristic sweet taste

¹Hunan Huacheng states that the intended use of SGFJC excludes infant formula and foods under the U.S. Department of Agriculture's jurisdiction.

to SGFJC are cucurbitane glycosides known as mogrosides, primarily mogroside V (CAS Registry Number 88901-36-4). Hunan Huacheng describes four SGFJC formulations that contain mogroside V at levels ranging from $\geq 0.6\%$ to $\geq 3.9\%$. These SGFJC formulations contain water and other components of *S. grosvenorii* fruit, such as carbohydrates, fiber, and protein.

Hunan Huacheng describes the manufacturing process for SGFJC. *S. grosvenorii* fruits are washed and crushed. The crushed fruits are extracted with hot water, then filtered. The extract is deionized using ion-exchange chromatography and then concentrated under vacuum to 10, 40, 50, or 65 °Brix. The concentrated solution is sterilized to obtain the final SGFJC formulation. Hunan Huacheng states that all materials used in the manufacture of SGFJC are food grade and meet applicable regulations, and that the manufacturing process is consistent with current good manufacturing practices.

Hunan Huacheng provides specifications for four SGFJC formulations that include a minimum content of mogroside V for each formulation ($\geq 0.6\%$, $\geq 2.4\%$, $\geq 3.1\%$, and $\geq 3.9\%$) and limits on moisture ($< 90\%$, $< 60\%$, $< 50\%$, and $< 35\%$, respectively). Specifications for all SGFJC formulations include limits for arsenic (≤ 0.2 mg/kg), cadmium (≤ 0.15 mg/kg), lead (≤ 0.5 mg/kg), as well as limits on microorganisms. Hunan Huacheng provides results from three non-consecutive batch analyses conducted with each formulation to demonstrate that SGFJC can be manufactured to meet the specifications.

Hunan Huacheng provides estimates of dietary exposure to SGFJC and mogroside V based on the intended use in food. Hunan Huacheng states that the use of SGFJC in food is substitutional, on the basis of mogroside V, for the use of other ingredients obtained from *S. grosvenorii*; therefore, an increase in cumulative exposure is not expected. Based on estimates of dietary exposure provided in GRN 000556,² Hunan Huacheng reports that upper ($\geq 90^{\text{th}}$) percentile dietary exposures to mogroside V for healthy adults, diabetic adults, healthy children, and diabetic children are up to 1.05, 1.40, 1.55, and 1.42 mg/kg body weight (bw)/day, respectively. Based on the relative concentrations of mogroside V in SGFJC formulations, Hunan Huacheng calculates that the upper ($\geq 90^{\text{th}}$) percentile dietary exposures to SGFJC for healthy adults, diabetic adults, healthy children, and diabetic children are up to 175.0, 233.3, 258.3, 236.6 mg/kg bw/day, respectively.

Hunan Huacheng discusses dietary exposure to SGFJC and mogroside V from the intended use in infant and toddler foods. Hunan Huacheng states that the level of use of SGFJC is limited only by current good manufacturing practices; however, SGFJC would typically be used in infant and toddler foods at levels of 0.25%–0.5%. Based on a use level of 0.5% and consumption data from the 2011–2014 National Health and Nutrition

²GRN 000556 describes the use of *S. grosvenorii* fruit extract (containing $\geq 12.5\%$, $\geq 20\%$, $\geq 25\%$, $\geq 30\%$, $\geq 40\%$, $\geq 50\%$, $\geq 55\%$, or $\geq 90\%$ mogroside V) in foods. FDA evaluated this notice and responded in a letter dated June 17, 2015, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

Examination Survey and estimates of median bodyweight, Hunan Huacheng calculates that the highest 90th percentile estimate of dietary exposure to SGFJC is 125 mg/kg bw/day among 8 to 12-month-old infants. Based on a level of 3.9% mogroside V in SGFJC, Hunan Huacheng concludes that the highest estimated 90th percentile dietary exposure to mogroside V is 4.88 mg/kg bw/day among 8 to 12-month-old infants.

Hunan Huacheng discusses the safety of SGFJC, incorporating into the notice the safety data presented in the previous GRAS notices for the use of *S. grosvenorii* Swingle fruit juice concentrate and fruit extracts, in which the mogroside V concentration ranges from 3.5% to ≥95%.³ Hunan Huacheng performed an updated literature search through May 2018 that resulted in one new published study on the metabolism of mogroside V in healthy and type 2 diabetic rats. Hunan Huacheng states that the results of this study do not raise any concerns regarding the safety of SGFJC under its intended conditions of use. In addition, Hunan Huacheng provides the data from an unpublished report that includes an acute oral toxicity study and a bacterial reverse mutation assay conducted with SGFJC (containing ≥0.6% or ≥3.9% mogroside V). Hunan Huacheng states that these studies corroborate the earlier findings described in the previous GRAS notices.

Based on the information presented in the notice, Hunan Huacheng concludes that SGFJC is GRAS for its intended use in foods.

Standards of Identity

In the notice, Hunan Huacheng states its intention to use SGFJC in several food categories, including foods for which standards of identity exist, located in Title 21 of the Code of Federal Regulations. 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.

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 section 301(ll)(1)-(4) applies. In our evaluation of Hunan Huacheng's notice concluding that SGFJC 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 SGFJC. Accordingly, our response should not be construed to be a statement that foods containing SGFJC, if

³*S. grosvenorii* Swingle (Luo Han Guo) fruit juice concentrate and fruit extracts (containing various amounts of mogroside V) were the subjects of GRNs 000301, 000359, 000522, 000556, 000627, and 000706. We evaluated these notices and responded in letters dated June 15, 2010, April 11, 2011, December 8, 2014, June 17, 2015, October 11, 2016, and August 17, 2017, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

introduced or delivered for introduction into interstate commerce, would not violate section 301(I).

Conclusions

Based on the information that Hunan Huacheng provided, as well as other information available to FDA, we have no questions at this time regarding Hunan Huacheng's conclusion that SGFJC is GRAS under its intended conditions of use. This letter is not an affirmation that SGFJC 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 000784 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

**Michael A.
Adams -S**

Dennis M. Keefe, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

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