



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

Re: GRAS Notice No. GRN 000706

Dear Dr. Cho:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000706. We received the notice you submitted on behalf of Hunan Nutramax, Inc. (Hunan Nutramax) on May 15, 2017 and filed it on June 2, 2017. We received an amendment to the notice on July 3, 2017 that corrected a typographical error in the notice.

The subject of the notice is *Siraitia grosvenorii* Swingle (Luo Han Guo) fruit extract (containing  $\geq 25\%$ ,  $\geq 30\%$ ,  $\geq 50\%$ ,  $\geq 55\%$ ,  $\geq 60\%$ ,  $\geq 65\%$ , or  $\geq 95\%$  mogroside V) (SGFE) for use as a table top sweetener and a general purpose sweetener in foods, at levels determined by current good manufacturing practices.<sup>1</sup> The notice informs us of Hunan Nutramax's view that these uses of SGFE are GRAS through scientific procedures.

Our use of the term "*Siraitia grosvenorii* Swingle (Luo Han Guo) fruit extract" or "SGFE" 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 Code of Federal Regulations (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 (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "*Siraitia grosvenorii* Swingle (Luo Han Guo) fruit extract" or "SGFE."

Hunan Nutramax provides information about the identity and composition of SGFE. SGFE is described as a mixture of compounds extracted from the *S. grosvenorii* Swingle fruit, commonly known as Luo Han Guo or monk fruit. The components of SGFE that are responsible for imparting the characteristic sweet taste to SGFE are cucurbitane glycosides known as mogrosides (II-VI). Mogroside V (CAS Reg. No. 88901-36-4) is the major mogroside component of SGFE. Hunan Nutramax describes seven SGFE formulations that contain mogroside V (at levels ranging from  $\geq 25\%$  to  $\geq 95\%$ ), as well as other components of the *S. grosvenorii* fruit, such as carbohydrates, fiber, and

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<sup>1</sup> Hunan Nutramax states that the intended use of SGFE excludes infant formula and foods under the U.S. Department of Agriculture's jurisdiction.

protein.

Hunan Nutramax describes the manufacturing process for SGFE. Unpeeled *S. grosvenorii* Swingle fruits are washed and crushed. The crushed fruits are extracted in hot water, and then the extract is cooled, centrifuged, and filtered. The extract is passed through an adsorption resin, which is washed and then desorbed with aqueous ethanol. The eluate is concentrated and spray dried to yield SGFE containing 18-32% mogroside V. Alternatively, the eluate may undergo additional steps, including treatment with an ion-exchange resin, silica gel chromatography, and membrane filtration. The products of these additional steps are concentrated and dried. The manufacturing process, including optional steps, results in five *S. grosvenorii* fruit extracts with differing concentrations of mogroside V (18% to 95%) that can be selectively mixed to produce seven SGFE formulations with mogroside V concentrations ranging from  $\geq 25\%$  to  $\geq 95\%$ . Hunan Nutramax states that the ethanol, ion-exchange resins, and adsorption resin used are food grade and meet applicable regulations.

Hunan Nutramax provides specifications for the SGFE formulations that include a minimum content of mogroside V for each formulation ( $\geq 25\%$ ,  $\geq 30\%$ ,  $\geq 50\%$ ,  $\geq 55\%$ ,  $\geq 60\%$ ,  $\geq 65\%$ , and  $\geq 95\%$ ), limits on moisture ( $< 5.0\%$ ), ethanol ( $\leq 500$  mg/kg), arsenic ( $\leq 0.5$  mg/kg), cadmium ( $\leq 0.05$  mg/kg), mercury ( $\leq 0.1$  mg/kg), and lead ( $\leq 0.5$  mg/kg). Specifications also include limits on microbial contaminants. Hunan Nutramax provides results from three non-consecutive batch analyses conducted with each formulation to demonstrate that SGFE meets the specifications.

Hunan Nutramax provides an estimate of dietary exposure to SGFE. Hunan Nutramax determined the relative sweetness of the seven SGFE formulations to be in the range of 160 to 420 times that of sucrose. Using these relative sweetness intensities and the methodology described in GRN 000301,<sup>2</sup> Hunan Nutramax calculates dietary exposures to SGFE and mogroside V for each of the SGFE formulations and for different subpopulations. The reported mean and upper ( $\geq 90^{\text{th}}$ ) percentile dietary exposures to SGFE for healthy adults are up to 1.6 and 4.2 mg/kg body weight (bw)/day, respectively. The reported mean dietary exposures to mogroside V for healthy adults, diabetic adults, healthy children, and diabetic children are up to 0.58, 0.63, 0.96, and 1.52 mg/kg bw/day, respectively, and the 90<sup>th</sup> percentile exposures are up to 1.53, 2.03, 2.24, and 2.05 mg/kg bw/day, respectively. Hunan Nutramax states that SGFE will replace other *S. grosvenorii* fruit extracts in the marketplace; therefore, an increase in cumulative dietary exposure is not expected. Hunan Nutramax states that SGFE is self-limiting due to a lack of palatability with increasing quantity.

Hunan Nutramax discusses the safety of SGFE by incorporating the safety data presented in GRNs 000301, 000359, 000522, and 000556 into the notice.<sup>2</sup> The mogroside V concentrations in SGFE described in these notices range from 12.5% to 90%. Hunan Nutramax includes an update of the literature through March 2017 that revealed one new clinical study. Hunan Nutramax discusses this published study that

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<sup>2</sup> SGFE was the subject of GRNs 000301, 000359, 000522, and 000556. We evaluated these notices and responded in letters dated January 15, 2010; April 11, 2011; December 8, 2014; and November 5, 2015, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

compares the effects of consuming non-nutritive sweeteners (aspartame, SGFE, and stevia-sweetened beverages) and sucrose on total daily energy intake, postprandial blood glucose and insulin response. The authors concluded that the consumption of non-nutritive sweeteners had no influence on the parameters studied. The notifier states that no adverse effects from SGFE were reported.

To further support the safety of SGFE, Hunan Nutramax describes the long history of safe consumption of Luo Han Guo fruit and its preparations in foods in China. Moreover, Hunan Nutramax notes the decision by Health Canada's Food Directorate to authorize the use of SGFE (at a maximum use level of 0.8% mogroside V content) in tabletop sweeteners. Based on its consideration of all the available data and information, Hunan Nutramax concludes that SGFE is GRAS under the conditions of its intended use.

### **Standards of Identity**

In the notice, Hunan Nutramax states its intention to use SGFE in several food categories, including foods for which standards of identity exist, located in Title 21 of the 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, and 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). The notice raises a potential issue under these labeling provisions. Hunan Nutramax cites studies that describe SGFE as having certain health benefits. If products containing SGFE 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 ONFL. OFAS 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.

### **Section 301(II) of the FD&C Act**

Section 301(II) 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(II)(1)-(4) applies. In our evaluation of Hunan Nutramax's notice concluding that SGFE is GRAS under its intended conditions of use, we did not consider whether section 301(II) or any of its exemptions apply to foods containing SGFE. Accordingly, our response should not be construed to be a statement that foods containing SGFE, if

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

### **Conclusions**

Based on the information that Hunan Nutramax provided, as well as other information available to FDA, we have no questions at this time regarding Hunan Nutramax's conclusion that SGFE is GRAS under its intended conditions of use. This letter is not an affirmation that SGFE 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 000706 is accessible to the public at [www.fda.gov/grasnoticeinventory](http://www.fda.gov/grasnoticeinventory).

Sincerely,

Michael A. Adams

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Dennis M. Keefe, Ph.D.

Director

Office of Food Additive Safety

Center for Food Safety

and Applied Nutrition

Digitally signed by Michael A. Adams -S  
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