Anne Petersen
Nestec S.A.
Avenue Nestlé 55
CH-1800 Vevey
SWITZERLAND

Re: GRAS Notice No. GRN 000792

Dear Ms. Petersen:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000792. We received Nestec S.A. (Nestec)'s GRAS notice on June 26, 2018 and filed it on July 25, 2018. We received an amendment to the notice on November 27, 2018,[1] containing additional information relating to the use of the notified substance in products under USDA jurisdiction.

The subject of the notice is *Corynebacterium glutamicum* corn syrup fermentation product for use as a flavoring agent in gravies and sauces, herb and spice mixes, and seasonings,[2] relishes, mayonnaise-like products,[3] meat and fish analogues, and soups and broths, at use levels of up to 0.76% of the final food as consumed. The notice informs us of Nestec's view that these uses of *C. glutamicum* corn syrup fermentation product are GRAS through scientific procedures.

Our use of the term "*Corynebacterium glutamicum* corn syrup fermentation product" 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 (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "*Corynebacterium glutamicum* corn syrup fermentation product."

Nestec provides information about the identity and composition of *C. glutamicum* corn

[1] The November 27, 2018, amendment included data that Nestec designated confidential. The Food Safety and Inspection Service of USDA advises that this data was not a factor in their review as the accompanying narrative was sufficient.
[2] The gravies and sauces, herb and spice mixes, and seasonings, may be added to meat- and poultry-containing finished foods under jurisdiction of USDA.
[3] The notifier indicated that this food use represents non-standardized mayonnaise products.

syrup fermentation product. *C. glutamicum* corn syrup fermentation product is a pale brown to brownish paste, which is composed of glutamic acid, L-alanine, succinic acid, formic acid, and an intrinsic mix of other free and bound amino acids, organic acids, Amadori and Maillard products, and minerals and their salts.

Nestec describes the method of manufacture for *C. glutamicum* corn syrup fermentation product. A pure culture of *C. glutamicum* strain 534[4] is fermented under controlled conditions in media containing corn glucose syrup, which is produced by enzymatic[5] hydrolysis of corn starch. Following fermentation, the fermentation product is heated and filtered to inactivate and remove the bacteria. The fermentation product is vacuum evaporated and sodium chloride is added. Nestec states that all reagents and processing aids used in the manufacture of are food grade and the method is conducted in accordance with current good manufacturing practices.

Nestec provides specifications for *C. glutamicum* corn syrup fermentation product that include moisture (27-34%), limits for heavy metals, including lead (<0.02 mg/kg), arsenic (≤0.5 mg/kg), and mercury (<0.004 mg/kg), as well as limits for microorganisms, including *Salmonella* serovars (absent in 25 g sample). Nestec provides the results of five non-consecutive batch analyses of *C. glutamicum* corn syrup fermentation product to demonstrate that it can be manufactured to meet these specifications.

Nestec provides estimates of dietary exposure to *C. glutamicum* corn syrup fermentation product based on the intended use level. Nestec estimates on a consumer-only basis, the mean and 90th percentile exposure to *C. glutamicum* corn syrup fermentation product to be 197 mg/person (p)/day (d) (3.2 mg/kg body weight (bw)/d) and 477 mg/p/d (7.8 mg/kg bw/d), respectively.

To support the safety of the intended uses of *C. glutamicum* corn syrup fermentation product, Nestec discusses published toxicological studies, the composition of the ingredient, and the safety of the *C. glutamicum* fermentation organism. Nestec discusses the results of a published 90-day subchronic oral toxicity study in rats using a mixture of *C. glutamicum* corn syrup fermentation product and *C. stationis* corn syrup fermentation product at a 2:1 ratio, respectively.[6] Nestec concludes that no treatment-related adverse effects occurred at the highest level of the mixture tested, 3,500 mg/kg bw/d, which is equivalent to approximately 2,333 mg/kg bw/d *C. glutamicum* corn syrup fermentation product. Nestec discusses the results of a published 14-day acute study in rats at up to 2,000 mg/kg bw/d *C. glutamicum* corn syrup fermentation product and reports that no treatment-related adverse effects were observed. Nestec

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[4] Nestec states that the strain is deposited in culture collections including ATCC as *C. glutamicum* ATCC 13032.

[5] Nestec states that the glucoamylase, alpha-amylase, and glucose isomerase enzymes used to hydrolyze corn starch are safe and suitable for such use.

[6] *C. stationis* corn syrup fermentation product is the subject of GRN 000793; GRN 000792 and GRN 000793 were reviewed concurrently.

also cites a published bacterial reverse mutation assay and chromosomal aberration test using human blood peripheral lymphocytes and concludes that *C. glutamicum* corn syrup fermentation product is not mutagenic or clastogenic.

Nestec states that *C. glutamicum* corn syrup fermentation product is mainly composed of amino acids, minerals, water, sugars, and organic acids that are normal components of the human diet and are expected to be digested and metabolized in a similar manner to other commonly consumed nutrients. Nestec also summarizes available safety information for each of the major constituents: glutamic acid, L-alanine, formic acid, and succinic acid.

Nestec states that *C. glutamicum* is a non-pathogenic, non-toxigenic organism commonly used in the food production.

Nestec includes the statement of a panel of individuals (Nestec's GRAS panel). Based on its review, Nestec's GRAS panel concluded that *C. glutamicum* corn syrup fermentation product is safe under the conditions of its intended use.

Based on the data and information described above, Nestec concludes that *C. glutamicum* corn syrup fermentation product is GRAS for its intended uses.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, Nestec notes that *C. glutamicum* corn syrup fermentation product has a brown to brownish color. As such, the use of *C. glutamicum* corn syrup fermentation product in food products may constitute a color additive use under section 201(t)(1) of the Food Drug & 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 000792 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 Petition Review in OFAS.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 000792, we coordinated with the Food Safety and Inspection Service (FSIS) of the USDA. Under the Federal Meat Inspection Act, the Poultry Products Inspection Act, and the Egg Products Inspection Act, FSIS determines the efficacy and suitability of ingredients used in meat, poultry, and egg products, and prescribes safe conditions of use. Suitability relates to the ingredient's effectiveness in performing its intended technical effect and the assurance that the ingredient's use will not result in products that are adulterated or misleading

for consumers.

FSIS has completed its review and has no objection to the use *Corynebacterium glutamicum* corn syrup fermentation product intended for use as a flavoring agent in sauces and gravies in meat and poultry at levels of up to 0.76% in the finished food product.

Regarding labeling, any establishment which uses this product is required to label the ingredient corn sauce (cultured corn syrup, water, salt) or corn sauce (cultured corn glucose syrup, water, salt) in the ingredients statement of the products in which it is used in.

Please contact Ms. Rosalyn Murphy-Jenkins at (301) 504-0879 or via email at Rosalyn.Murphy-Jenkins@usda.gov if you have questions regarding labeling.

Any additional questions regarding regulatory guidance from FSIS should be directed to: Melanie Abley, Acting Deputy Director, Risk Management and Innovations Staff, Office of Policy and Program Development, Food Safety and Inspection Service, at (202) 690-6573 or via email at Melanie.Abley@usda.gov.

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 Nestec's notice concluding that *C. glutamicum* corn syrup fermentation product 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 *C. glutamicum* corn syrup fermentation product. Accordingly, our response should not be construed to be a statement that foods containing *C. glutamicum* corn syrup fermentation product, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Nestec provided, as well as other information available to FDA, we have no questions at this time regarding Nestec's conclusion that *C. glutamicum* corn syrup fermentation product is GRAS under its intended conditions of use. This letter is not an affirmation that *C. glutamicum* corn syrup fermentation product 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 000792 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Michael A. Adams -S

Digitally signed by Michael A. Adams -S
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Dennis M. Keefe, Ph.D.
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