Frederick Stearns
Keller and Heckman LLP
1001 G Street, NW
Suite 500 West
Washington, DC 20001

Re: GRAS Notice No. GRN 001123

Dear Mr. Stearns:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001123. We received the notice that you submitted on behalf of Mitsubishi Chemical Corporation (Mitsubishi) on November 3, 2022, and filed it on April 12, 2023. Mitsubishi submitted amendments to the notice on July 21, 2023, August 15, 2023, and September 28, 2023, clarifying information on the analytical methods and batch analyses, reducing specifications for heavy metals, and providing additional information on the dietary exposure assessment and an additional discussion for safety in children aged 2 to 11 years.

The subject of the notice is sucrose fatty acid esters (SFAE) for use as an emulsifier or stabilizer in chocolate and chocolate-containing products, including imitation and chocolate substitute products, at a maximum use level of 0.3%. The notice informs us of Mitsubishi's view that these uses of SFAE are GRAS through scientific procedures.

Mitsubishi describes SFAE as white to yellow-brown powders, grains, or flakes containing ≥ 80% mono-, di-, and tri-esters of sucrose with fatty acids.

Mitsubishi describes the manufacturing process for SFAE by inter-esterification of sucrose with methyl esters of fatty acids, derived from edible vegetable or hydrogenated edible vegetable oils and fats, in the presence of solvents, including ethyl acetate, methyl ethyl ketone, dimethyl sulfoxide, or isobutanol. Mitsubishi notes that the ratio of methyl esters of fatty acids to sucrose establishes the degree of esterification. Mitsubishi states that following esterification, the crude reaction product is dissolved in a solvent and then purified via water extraction. Mitsubishi states that the purification product is either freeze dried, filled, and packaged, or dehydrated, cooled, and flaked; if following the latter process steps, the substance is subsequently either filled and packaged, or pulverized, filled, and packaged. Mitsubishi states that SFAE is manufactured using food grade materials and processing aids and is produced in compliance with the applicable U.S. food safety requirements, including current good manufacturing practices.

Mitsubishi provides specifications for SFAE that include assay (≥ 80%), free sucrose (≤ 4%), acid value (≤ 5%), lead (≤ 0.1 mg/kg), arsenic (≤ 0.1 mg/kg), cadmium (≤ 0.1

mg/kg), mercury (≤ 0.1 mg/kg), methyl ethyl ketone (≤ 10 mg/kg), ethyl acetate (≤ 350 mg/kg), methanol (≤ 10 mg/kg), dimethylsulfoxide (≤ 2 mg/kg), isobutanol (≤ 10 mg/kg), moisture (≤ 4%), and residue on ignition (≤ 1.5%), and limits for microorganisms. Mitsubishi provides the results from the analyses of three non-consecutive batches to demonstrate that SFAE can be manufactured to meet the specifications. Mitsubishi demonstrates that SFAE is stable for at least 30 months when stored unopened in a dark, well-ventilated space at a temperature from 10–35 °C.

Mitsubishi estimates an eaters-only dietary exposure to SFAE from the proposed uses to be 93 mg/person(p)/d (1.5 mg/kg bw/d) at the mean and 213 mg/p/d (3.6 mg/kg bw/d) at the 90th percentile for the U.S. population aged 2 years or older using food consumption data from the 2017-2018 National Health and Nutrition Examination Survey (NHANES). Mitsubishi also estimates an eaters-only cumulative dietary exposure to SFAE from all current and proposed uses to be 650 mg/p/d (9.8 mg/kg bw/d) at the mean and 1,277 mg/p/d (20 mg/kg bw/d) at the 90th percentile for the U.S. population aged 2 years and older.

Mitsubishi reports the published data supporting the safe use of SFAE in foods and discusses that previous GRAS notices (GRNs 000129, 000248, 000421, and 000514)[1] have also evaluated the safety of SFAE. These data include, but were not limited to, a two-year combined chronic oral toxicity and carcinogenicity study in rats and two human tolerance studies. Mitsubishi reviews the two-year combined chronic toxicity and carcinogenicity study that reports no adverse effects[2] of 5% SFAE in the diet. Mitsubishi notes the first human tolerance study, in which treatment-related soft stool or diarrhea were observed in multiple study groups, had significant deficiencies, including the limited size of study groups and lack of controls. Mitsubishi reviews the second human tolerance study that reports no adverse effects of daily doses of 1.5 g SFAE for 5 days.

Mitsubishi discusses the absorption, distribution, metabolism and excretion of SFAE and states that it is extensively hydrolyzed by pancreatic lipase in the gastrointestinal tract into sucrose and fatty acids prior to absorption, that only small amounts of intact monoesters are absorbed, that incompletely hydrolyzed sucrose esters appeared to be excreted in the feces, and that there was no evidence of tissue accumulation of the absorbed monoesters, which are completely metabolized to carbon dioxide or integrated into other endogenous constituents. Mitsubishi discusses the potential limit of safe dietary exposure for children aged 2 to 11 years. Mitsubishi states that it is expected that children aged 11 years and younger would metabolize SFAE comparably with adults. Mitsubishi also states that little to no difference for the dietary exposure is expected compared to the estimates discussed in GRN 000514, and Mitsubishi notes any increase is not expected to result in adverse effects in children or the general population. Mitsubishi notes that an updated search of the literature through November 2022 did

[1] SFAE was the subject of GRNs 000129, 000248, 000421, and 000514. We evaluated these notices and responded in letters dated November 7, 2003, October 24, 2008, August 10, 2012, and December 3, 2014, respectively, stating that we had no questions at those times regarding the notifiers' GRAS conclusions.
[2] Mitsubishi notes that treatment-related effects reported in this study were considered by the authors to be small and not considered toxicologically relevant.

not identify any new information that raises safety concerns.

Based on the totality of the data and information, Mitsubishi concludes that SFAE is GRAS under its intended conditions of use.

Standards of Identity

In the notice, Mitsubishi states its intention to use SFAE 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 Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, Mitsubishi describes SFAE as white to yellow-brown powders, grains, or flakes. As such, the use of SFAE 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 001123 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 the Office of Food Additive Safety.

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 Mitsubishi's notice concluding that SFAE 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 SFAE. Accordingly, our response should not be construed to be a statement that foods containing SFAE, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Mitsubishi provided, as well as other information available to FDA, we have no questions at this time regarding Mitsubishi's conclusion

that SFAE is GRAS under its intended conditions of use. This letter is not an affirmation that SFAE 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 170.257(b)(2), the text of this letter responding to GRN 001123 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.11.03 12:09:48 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
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