



Sylvia Bergman, Ph.D.
Kemin Industries, Inc. d/b/a Kemin Food Technologies
2100 Maury Street
Des Moines, IA 50317

Re: GRAS Notice No. GRN 000772

Dear Dr. Bergman:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000772. We received Kemin Industries, Inc. d/b/a Kemin Food Technologies (Kemin)'s notice on March 23, 2018, and filed it on April 23, 2018. Kemin submitted amendments to the notice on May 31, 2018, September 28, 2018, October 2, 2018, and November 30, 2018, that include additional information regarding the manufacturing process, composition, specifications, and analytical methods, a revised Part 1 of the notice stating that Kemin's GRAS panel had access to confidential information not included in the notice, and a revised section of the notice that discusses this panel.¹

The subject of the notice is palmitoylated green tea catechins (PGTC) for use as an antioxidant in baked goods and baking mixes; breakfast cereals; cheeses; confections and frostings; dairy product analogs; fats and oils; grain products and pastas; herbs, seeds, spices, seasonings, blends, extracts, and flavorings; nut and nut products; snack foods; and soft candies at levels up to 0.28%. Intended uses exclude food products for which a standard of identity does not permit the use of PGTC. The notice informs us of Kemin's view that the use of PGTC is GRAS through scientific procedures.

Our use of the term "palmitoylated green tea catechins" 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

¹ Part 1 of the notice received on March 23, 2018, does not state that Kemin's GRAS panel had access to confidential information not included in the notice. To address this issue, FDA provided Kemin an option of revising Part 1 and the section of the notice that discusses the GRAS panel and submitting it as an amendment in which Part 1 described the confidential information provided to Kemin's GRAS panel and explains how there could be a basis for a conclusion of safety if qualified experts do not have access to this information.

(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 “palmitoylated green tea catechins.”

Kemin provides information about the identity and composition of PGTC. Kemin states that PGTC consists primarily of palmitoylated catechins (66–82% expressed as epigallocatechin gallate (EGCG) monopalmitate equivalents) and free palmitic acid (10–15% w/w) with small amounts (<2% w/w combined) of free catechins, gallic acid, and alkaloids (caffeine, theobromine, and theophylline). Kemin states that approximately 57% (w/w) of the total palmitoylated catechins is green tea catechins and 30% (w/w) is EGCG. PGTC is designated by the CAS Registry Number 1448315-04-5.

Kemin describes the manufacturing process for PGTC. Green tea catechins are obtained by solvent extraction from a decaffeinated hot aqueous infusion of *Camellia sinensis* L. leaves. The extract is then reacted with a source of palmitic acid in the presence of a metal catalyst. The crude reaction product is filtered to remove the catalyst, washed, purified, concentrated by evaporation, and then crystallized and freeze-dried resulting in the finished PGTC product. Kemin states that the green tea leaves, palmitic acid, and the catalyst are food grade, and the manufacturing process is consistent with current good manufacturing practice.

Kemin provides specifications for PGTC. These include a purity assay (66–82% expressed as EGCG monopalmitate equivalents), moisture content ($\leq 5\%$), residual ash ($\leq 1\%$), limits for arsenic (≤ 2 mg/kg), cadmium (≤ 1 mg/kg), mercury (≤ 0.1 mg/kg), lead (≤ 1 mg/kg), total trace elements (copper, iron, manganese, sodium and zinc) (≤ 250 mg/kg), and microbial contaminants. Kemin provides results of three non-consecutive batch analyses to demonstrate that PGTC can be manufactured to meet specifications and states that routine batch analyses are conducted to ensure that the levels of residual solvents, residual catalyst, dioxins, polychlorinated biphenyls, and pesticides are within acceptable limits. Kemin states that PGTC is stable for at least three years when stored under defined conditions.

Kemin provides an estimate of the dietary exposure to PGTC based on the intended uses in food at the maximum use level and food consumption data from the National Health and Nutrition Examination Survey (NHANES; 2011–2012). Kemin reports that the dietary exposure to PGTC for the total U.S. population (users only) is estimated to be 135 mg/person(p)/day(d) (2.3 mg/kg body weight (bw)/d) at the mean and 270 mg/p/d (5.0 mg/kg bw/d) at the 90th percentile.

Based on results of studies indicating that PGTC would be hydrolyzed to green tea catechins and palmitic acid in the body, Kemin provides estimates of dietary exposure to green tea catechins and EGCG from the intended uses of PGTC. The dietary exposure to green tea catechins is estimated to be 63 mg/p/d (equivalent to 1.05 mg/kg bw/d, based on a 60 kg adult) at the mean and 126 mg/p/d (2.1 mg/kg bw/d) at the 90th percentile. The dietary exposure to EGCG is estimated to be 33 mg/p/d (0.55 mg/kg bw/d) at the mean and 66 mg/p/d (1.1 mg/kg bw/d) at the 90th percentile. Kemin states that these estimates are lower than the amounts of green tea catechins and EGCG typically

consumed from a 240 mL serving of green tea (i.e., 316 mg and 168 mg, respectively). Kemin notes that the quantity of PGTC used would be self-limiting due to unpalatability.

Kemin discusses published and unpublished data and information supporting the safety of PGTC. Kemin summarizes published rat studies on the absorption, distribution, metabolism, and excretion of 3-palmitoyl-(+)-catechin, a representative form of PGTC. Kemin also discusses published and unpublished *in vitro* studies on PGTC performed in simulated gastric and intestinal environments. These studies indicate that PGTC would be hydrolyzed to green tea catechins and palmitic acid within two hours in the body. Green tea catechins and palmitic acid will be metabolized in the same manner as those from naturally occurring dietary sources. Kemin discusses published 30-day and 90-day oral toxicity studies in rats as well as an unpublished 84-day oral toxicity study in dogs. In the 30-day study, rats were administered PGTC by gavage at levels up to 2330 mg/kg bw/d. In the 90-day study, rats were fed diets estimated to provide PGTC at levels up to 500 mg/kg bw/d. In the 84-day study, dogs were fed diets estimated to provide PGTC at levels up to 50 mg/kg bw/d. Kemin reports that no adverse effects were observed in any of these studies. In addition, Kemin discusses the safety of the individual components of PGTC (i.e., green tea catechins and palmitic acid) under the intended conditions of use. The dietary exposure of palmitic acid is expected to be minimal in comparison to its exposure from dietary sources. Kemin discusses the liver toxicity associated with green tea catechins, particularly EGCG, and states that the exposure from the highest estimated dietary exposure to of PGTC is well below the range when compared to that of a serving of a cup of green tea (as described above). Further, it is supported by the absence of liver toxicity or other adverse events in the 90-day oral toxicity study in rats using PGTC at levels up to 500 mg/kg bw/d. Based on the results of the published genotoxicity studies, Kemin states that PGTC is neither mutagenic nor genotoxic.

Based on the data and information presented in the notice, Kemin concludes that PGTC is GRAS for its intended use in foods.

We note that GRN 000772 referred to a panel of individuals (Kemin's GRAS panel). The notice did not provide a GRAS panel report. Kemin stated that the report contained confidential information and offered to provide a redacted version of the GRAS panel report, which FDA declined. Nonetheless, because the notice provided publicly available information supporting Kemin's conclusion, we completed our evaluation without the deliberations of Kemin's GRAS panel.

Potential Labeling Issues

Under section 403(k) of the Food, Drug, and Cosmetic Act (FD&C Act), a food is misbranded if it contains any chemical preservative, unless the label states that fact. Under section 403(i)(2) of the FD&C Act, a food is misbranded unless its label bears the common or usual name of each ingredient. Further, under section 403(a) of the FD&C Act, a food is misbranded if its labeling is false or misleading in any way. Kemin's intended use of PGTC constitutes use as a preservative. Therefore, the ingredient statement on labels of food products containing PGTC must comply with the labeling regulations implemented in sections 403(k) and 403(i)(2) of the FD&C Act. For

example, 21 CFR 101.22(j) requires that the label of a food with an added chemical preservative must declare both the common or usual name of the ingredient and a separate description of its function. Further, food that is subjected to any form of preservation, except as provided in 21 CFR 101.95(c), may not be labeled as “fresh.” 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 Kemin’s notice concluding that PGTC 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 PGTC. Accordingly, our response should not be construed to be a statement that foods containing PGTC, if introduced or delivered for introduction into interstate commerce, would not violate section 301(II).

Conclusions

Based on the information that Kemin provided, as well as other information available to FDA, we have no questions at this time regarding Kemin’s conclusion that PGTC is GRAS under its intended conditions of use. This letter is not an affirmation that PGTC 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 000772 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

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