



Ashish Talati
Amin Talati Wasserman, LLP
100 S. Wacker Drive
Suite 2000
Chicago, IL 60606

Re: GRAS Notice No. GRN 000868

Dear Mr. Talati:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000868. We received the notice that you submitted on behalf of VDF FutureCeuticals, Inc. (VDF) on June 10, 2019, and filed it on August 19, 2019. VDF submitted an amendment to the notice on November 1, 2019, that clarified information related to the description of coffee fruit extract, batch compliance with specifications, dietary exposure, safety studies, and analytical method validation.

The subject of the notice is coffee fruit extract for use as an ingredient and as an antioxidant in certain beverages, including flavored waters, coffee, tea, ready-to-mix (RTM) beverages, fruit juices, and vegetable juices/blends; nutritional and replacement milk products (pre-workout); clusters/bars; chocolate; candy; and chewing gum, at levels ranging from 20 mg to 300 mg/serving.¹ This notice informs us of VDF's view that these uses of coffee fruit extract are GRAS through scientific procedures.

Our use of the term, "coffee fruit extract" 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 "coffee fruit extract."

VDF describes coffee fruit extract as a tan-brown powder derived from the coffee fruit of the plant *Coffea arabica*. Coffee fruit extract is extracted from the dried whole ground coffee fruit (including the coffee bean) using 70% aqueous ethanol and is composed of > 40% phenolic acids, with the remainder being caffeine, moisture, ash, carbohydrates, protein, and organic acids. VDF provides tables in the notice that list the characteristics

¹ VDF states that coffee fruit extract is not intended for use in infant formula, alcoholic beverages, foods under jurisdiction of the USDA, or where standards of identity preclude its use.

of coffee fruit extract and of the taxonomical classification of the source material, *C. arabica*.

VDF describes the method of manufacture for coffee fruit extract, which starts with the whole coffee fruit (exocarp, pulp, mucilage and the seed (or bean)). Whole coffee fruits are washed, dried, milled to the appropriate size, and extracted with 70% aqueous ethanol. The aqueous ethanolic extract is then filtered and concentrated by evaporation. The resulting product is subjected to a gravimetric phase separation to remove caffeine, autoclaved (98-100°C, 30 min), and spray-dried to produce the final coffee fruit extract powder containing $\geq 40\%$ phenolic acids and approximately 1-2% caffeine. VDF indicated that the coffee fruit extract is stable for 2 years at a storage temperature of 72 °F and a humidity of 55-60%.

VDF provides specifications for coffee fruit extract that include moisture ($\leq 10\%$), phenolic acids ($\geq 40\%$), caffeine (approximately 1-2%), residual ethanol (1000 mg/kg), aflatoxins ($< 4 \mu\text{g}/\text{kg}$, as a sum of B1, B2, G1, and G2), ochratoxin A ($< 10 \mu\text{g}/\text{kg}$), lead ($\leq 1 \text{mg}/\text{kg}$), arsenic ($\leq 1 \text{mg}/\text{kg}$), cadmium ($\leq 1 \text{mg}/\text{kg}$), mercury ($\leq 0.5 \text{mg}/\text{kg}$), and limits for microorganisms. VDF provides the results of 4 non-consecutive batch analyses to demonstrate that coffee fruit extract can be manufactured to meet the stated specifications. VDF also describes the oxygen radical absorbance capacity (ORAC) value of $\geq 6000 \mu\text{mol}$ trolox equivalents (TE) per gram to support the antioxidant potential of coffee fruit extract. The ORAC value is driven by the polyphenol concentration of the extract.

VDF provides an all-users exposure estimate for coffee fruit extract from the proposed uses of 170 mg/p/d at the mean and 393 mg/p/d at the 90th percentile for the U.S. population aged 2 years or older, using food consumption data from the combined 2009-2014 National Health and Nutrition Examination Survey (NHANES). VDF also provides an all-users exposure estimate for the U.S. population aged 2 years and older for caffeine (3.4 mg/p/d at the mean and 7.8 mg/p/d at the 90th percentile) and total polyphenols (204 mg/p/d at the 90th percentile) from the proposed use of coffee fruit extract.

Additionally, VDF addresses the cumulative exposure to caffeine from the proposed uses of coffee fruit extract and the background sources (food and dietary supplements). The cumulative all-users caffeine exposure is estimated to be 137 mg/p/d at the mean and 332 mg/p/d at the 90th percentile for the U.S. population aged 2 years and older. VDF concludes that the additional caffeine exposure of 7.8 mg/p/d at the 90th percentile from the proposed use of coffee fruit extract is minor compared to the background exposure to caffeine.

VDF discusses published data and information supporting the safety of coffee fruit extract. VDF describes published safety data and information on three coffee fruit preparations: a water/ethanol extract (the subject of this notice), a water extract, and whole coffee fruit powder. In a 90-day study, the water/ethanol extract showed no adverse effects at dietary concentrations of up to 5% (approximately 3,446 and 4,087 mg/kg body weight (bw)/d for male and female rats, respectively). Bacterial

mutagenicity studies and murine micronucleus tests demonstrated that none of the three products showed mutagenic or genotoxic potential.

As the article of commerce contains approximately 40% of phenolic acids as chlorogenic acids, VDF discusses published metabolism and safety studies on chlorogenic acid in addition to published safety data on caffeic acid, the toxicologically relevant metabolite of chlorogenic acid. No adverse effects were reported in a 3-week published study in which diets of rats were supplemented with 1% chlorogenic acid (approximately 1,000 mg/kg bw/d) and in a combined reproductive/developmental published toxicity study in which chlorogenic acid was administered intraperitoneally at doses up to 500 mg/kg bw/d to rats during gestational days 5 to 12. No neoplasms or hyperplastic lesions were reported in a published study in which hamsters were administered 30 mg chlorogenic acid/kg bw/d in the diet for 24 weeks. VDF also describes a published human clinical study. Although the human study was not designed as a safety study, no adverse effects were reported when subjects consumed 800 mg/d of coffee fruit extract (approximately 10.8 mg/kg bw/d) for 28 days.

VDF includes the report of a panel of individuals (VDF's GRAS panel). Based on its review, VDF's GRAS panel concluded that coffee fruit extract is safe under the conditions of its intended use.

Based on the totality of the available scientific information, VDF concludes that coffee fruit extract is GRAS for its intended use.

Standards of Identity

In the notice, VDF states its intention to use coffee fruit extract 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.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and Cosmetic Act (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). If products containing coffee fruit extract 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.

Under section 403(k) of the 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. VDF's intended use of coffee fruit extract as an antioxidant constitutes use as a preservative. Therefore, the ingredient statement on labels of food products containing coffee fruit extract as an antioxidant 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.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, VDF describes coffee fruit extract as tan-brown. As such, the use of coffee fruit extract in food products may constitute a color additive use under section 201(t)(1) of the 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 000868 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 OFAS.

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

Conclusions

Based on the information that VDF provided, as well as other information available to FDA, we have no questions at this time regarding VDF's conclusion that coffee fruit extract is GRAS under its intended conditions of use. This letter is not an affirmation that coffee fruit extract 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 000868 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

**Susan J.
Carlson -S**

Digitally signed by
Susan J. Carlson -S
Date: 2020.03.24
10:41:07 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition