Donald F. Schmitt, MPH
ToxStrategies, Inc.
931 W. 75th St., Suite 137, PMB 255
Naperville, IL 60565

Re: GRAS Notice No. GRN 000879

Dear Mr. Schmitt:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000879. We received the notice that you submitted on behalf of Yantai T. Full Biotech Co, Ltd. (TFULL) on July 17, 2019. In an email dated August 28, 2019, you excluded from the notice the intended use of the notified substance in meat and poultry products under the jurisdiction of USDA. We filed the notice on September 26, 2019. TFULL submitted amendments to the notice on November 21, 2019, and February 11, 2020, that corrected information listed in the table of specifications, clarified the manufacturing methods, and provided additional discussion regarding allergenicity and safety.

The subject of the notice is protein isolated from *Vicia faba* L. (fava bean protein isolate) at levels ranging from 10 to 90% of food as consumed for use as a protein source in bakery products; snack foods; beverages (including nutritional beverages); soups; imitation dairy products; meal replacement/nutritional bars; meat analogs; and dry-blend protein powders. The notice informs us of TFULL's view that these uses of fava bean protein isolate are GRAS through scientific procedures.

Our use of the term, "fava bean protein isolate," 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, "fava bean protein isolate."

TFULL provides information about the identity and composition of fava bean protein isolate. TFULL describes the fava bean protein isolate as an extract of fava beans (*V. faba* L.) consisting of ≥90% protein. The nutritional composition for fava bean protein isolate is protein (85%), moisture (7%), carbohydrates (3%), ash (3%), fat (2%), and sodium (0.6%). TFULL presents the amino acid profile of fava bean protein isolate and compares it to the amino acid profile of other common food-derived proteins.

TFULL provides a description of the manufacturing process for fava bean protein isolate. TFULL states that fava bean flour obtained from commercially available milled fava beans is soaked and extracted with purified water. The resulting slurry is separated by centrifugation and treated with hydrochloric acid to precipitate the protein. The protein precipitate is washed and neutralized by the addition of sodium hydroxide. The resulting fava bean protein is then sterilized, evaporated, homogenized, and spray dried. TFULL states that it uses processing aids that are safe and common to food ingredient manufacturing. TFULL states that fava bean protein isolate is manufactured in accordance with current good manufacturing practices.

TFULL provides specifications for fava bean protein isolate that include protein (≥90%), ash (≤5%), pH (6-7), lead (≤0.1 mg/kg), arsenic (≤0.1 mg/kg), cadmium (≤0.1 mg/kg), mercury (≤0.1 mg/kg), and limits for microorganisms. TFULL provides results from analyses of four non-consecutive production lots to demonstrate that fava bean protein isolate can be produced to meet these specifications. TFULL also provides concentrations of the anti-nutrient alkaloid components vicine, convicine, divicine, and isouramil from three lots of fava bean protein isolate. TFULL states that the soaking, acid hydrolysis, and sterilization steps of their manufacturing process significantly reduce vicine, convicine, divicine, isouramil, and active beta-glucosidase remaining in fava bean protein isolate. TFULL notes that L-3,4-dihydroxyphenylalanine (L-DOPA) naturally occurs in fava beans, but its levels decrease significantly in heated/cooked beans as has been reported in the literature. TFULL determined the level of L-DOPA in fava bean protein isolate to be 13.3 mg/kg by HPLC. TFULL states that fava bean protein isolate is stable for up to 24 months under typical shelf-life storage conditions, based on results from their stability studies.

TFULL notes previous GRAS conclusions for plant-based protein sources for identical food uses as a basis of dietary exposure. Specifically, TFULL refers to GRN 000575[1] which cites FDA's daily reference value for protein (50 g/person/day), protein intake recommendations from Dietary Guidelines for Americans (HHS/USDA, 2005), and acceptable protein intake ranges from the Institute of Medicine (IOM, 2005). In addition, TFULL references GRN 000581[2] to support the intended use of fava bean protein isolate. TFULL indicates that the intended uses are substitutional for other dietary sources of protein and thus are not expected to increase the overall consumption

[1] Oat protein was the subject of GRN 000575. We evaluated this notice and responded in a letter dated September 15, 2015 stating that we had no questions at that time regarding the notifier's GRAS conclusion.

[2] Un-hydrolyzed and hydrolyzed pea protein was the subject of GRN 000581. We evaluated this notice and responded in a letter dated March 20, 2016 stating that we had no questions at that time regarding the notifier's GRAS conclusion.

of protein. TFULL states that the use of fava bean protein isolate in protein enriched foods is self-limiting for technological reasons (i.e., product texture and flavor profile).

TFULL states that fava beans are considered inherently non-toxic due to a long history of safe consumption of appropriately-treated fava beans by humans. TFULL discusses publicly available information relevant to their safety determination based on a scientific literature search. TFULL summarizes the relevant published safety information from available animal and human studies. TFULL discusses the presence of anti-nutritional factors in untreated fava beans, such as vicine and convicine, whose metabolites induce favism in certain glucose-6-phosphate dehydrogenase deficient consumers. TFULL provides analytical data that support their conclusion that consumption of 50-60 g of fava bean protein isolate per day would not be expected to result in dietary exposure to levels of anti-nutrients that would elicit the adverse effects observed in people prone to favism. TFULL discusses published reports of fava bean allergenicity, and cross-reactivity with other allergens. However, TFULL notes that allergic reactions to fava beans and cross-reactivity with other allergens are rare and consistent with responses to other legumes; fava bean is not one of the eight major food allergens.

TFULL includes the report of a panel of individuals (TFULL's GRAS panel). Based on its review, TFULL's GRAS panel concluded that fava bean protein isolate is safe under the conditions of its intended use.

Based on the data and information, TFULL concludes that fava bean protein isolate is GRAS for its intended use.

Standards of Identity

In the notice, TFULL states its intention to use fava bean protein isolate 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). These 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(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 TFULL's notice concluding that fava bean protein isolate 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 fava bean protein isolate. Accordingly, our response should not be construed to be a statement that foods containing fava bean protein isolate, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that TFULL provided, as well as other information available to FDA, we have no questions at this time regarding TFULL's conclusion that fava bean protein isolate is GRAS under its intended conditions of use. This letter is not an affirmation that fava bean protein isolate 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)(1), the information in this notice described in 21 CFR 170.225(c)(2) through (c)(5) will be accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. -
Date: 2020.03.23 15:39:18 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
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