



Donald F. Schmitt, M.P.H.  
ToxStrategies, Inc.  
23501 Cinco Ranch Blvd., Suite B226  
Katy, TX 77494

Re: GRAS Notice No. GRN 001166

Dear Mr. Schmitt:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001166. We received the notice that you submitted on behalf of Nuritas on October 10, 2023 and filed it on March 25, 2024. Nuritas submitted amendments on July 10, 2024 and September 25, 2024, including clarifications on the intended uses, specifications, manufacturing process, dietary exposure, and literature search.

The subject of the notice is fava bean (*Vicia faba* L.) protein hydrolysate for use as a source of protein in select food categories at the maximum use levels specified in Table 1.<sup>1</sup> The notice informs us of Nuritas' view that this use of fava bean protein hydrolysate is GRAS through scientific procedures.

Table 1. Food categories and maximum use levels for fava bean protein hydrolysate

<b>Food categories</b>	<b>Maximum use level (%)</b>
Protein powders	30
Instant breakfast powders	12
Sport drink powders	7
Meal replacement drinks	1
Meal replacement bars	5
Milk analogs	1
Ready-to-drink (RTD) protein shakes	1
RTD sports drinks	1
Hard candies with vitamin C	12
Gummies with vitamin C	12
Protein bars	7
Energy bars	7
Cookies, dietetic or high fiber	7
Breakfast biscuit crackers	16

<sup>1</sup> Nuritas states that fava bean protein hydrolysate is not intended for use in infant formula or in products that are under the jurisdiction of the United States Department of Agriculture.

<b>Food categories</b>	<b>Maximum use level (%)</b>
Veggie burgers	6
Meatless fish sticks	2
Meatless pork/beef/chicken alternatives	2

Our use of the term, “fava bean protein hydrolysate” 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 non-standardized 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 Nutrition Center of Excellence (NCE). The Office of Pre-Market Additive Safety (OPMAS) did not consult with ONFL regarding the appropriate common or usual name for “fava bean protein hydrolysate”.

Nuritas describes fava bean protein hydrolysate as a light beige powder obtained from fava bean (*Vicia faba* L.) protein powder. Nuritas states that fava bean protein hydrolysate contains 55-65% protein, with the rest being moisture, carbohydrates, ash, and fat.

Nuritas describes the manufacturing process for fava bean protein hydrolysate. Fava bean protein powder (obtained by milling of fava bean seeds and dry fractionation) is suspended in an alkaline buffer and heated. The pH is adjusted to acidic conditions, if required, and a microbial-derived protease enzyme is added to catalyze the hydrolysis of the polypeptides. The enzyme is then deactivated under heat treatment prior to pasteurization and spray-drying. Nuritas states that all raw materials and processing aids are food grade and are used in accordance with applicable U.S. regulations or are GRAS for their intended uses, and that fava bean protein hydrolysate is manufactured in accordance with current good manufacturing practices.

Nuritas provides specifications for fava bean protein hydrolysate that include total protein (55-65% on a dry basis), moisture (3-8%), lead, mercury, arsenic and cadmium (each  $\leq 0.05$  mg/kg), and limits for microorganisms. Nuritas provides the results from the analyses of three non-consecutive batches to demonstrate that fava bean protein hydrolysate can be manufactured to meet these specifications. Nuritas states that fava bean protein hydrolysate is stable for at least 2 years when stored in a closed container in a cool dry place away from strong light.

Nuritas also determines the levels of the anti-nutrient alkaloid components, vicine and convicine, in three batches of fava bean protein hydrolysate. Results ranged from 0.54-14.1 mg/g for vicine and 0.16-4.7 mg/g for convicine. Nuritas also notes that L-3,4-dihydroxyphenylalanine (L-DOPA) occurs naturally in fava beans and states that the level of L-DOPA in the fava bean protein hydrolysate was approximately 1400 mg/kg.

Nuritas estimates the dietary exposure to fava bean protein hydrolysate from the

intended uses using food consumption data from the 2003-2016 National Health and Nutrition Examination Survey (NHANES). Nuritas estimates the eaters-only dietary exposure to fava bean protein hydrolysate to be 6.44 g/person (p)/d (99 mg/kg body weight (bw)/d) at the mean and 12.4 g/p/d (199 mg/kg bw/d) at the 90th percentile for the U.S. population aged 2 years and older. Nuritas states that the intended uses of fava bean protein hydrolysate will be substitutional for other sources of plant-based protein and therefore, the cumulative dietary exposure to protein is not expected to increase.

Nuritas states that fava beans and other legumes, and the protein from these sources, have been safely consumed as food and feed around the world for decades. Nuritas conducted a search of the literature on the safety of fava bean protein and notes that none of the publications found contradict its GRAS conclusion. Nuritas summarizes the available published animal toxicity studies on fava beans, fava bean protein, and fava bean protein hydrolysate and concludes that these studies demonstrate that there are not any safety concerns for these ingredients. Nuritas notes that fava beans naturally contain L-DOPA, a precursor to dopamine, a common treatment for Parkinson's disease. Nuritas states that the level of L-DOPA in fava bean protein hydrolysate is sufficiently below levels of safety concern. Nuritas also includes a discussion of the anti-nutrients found in fava beans, vicine and convicine, and their respective metabolites, aglycones divicine and isouramil. Nuritas notes that these compounds can produce "favism" in individuals who are genetically deficient in glucose-6-phosphate dehydrogenase (G6PD). However, Nuritas states this is not a safety concern for fava bean protein hydrolysate because the dietary exposure to these compounds from the intended uses would not elicit the effects observed in people prone to favism. Nuritas discusses the potential for fava bean protein hydrolysate to produce allergenicity in humans. Based on an assessment of the literature, Nuritas concludes that the possibility for fava bean proteins to cause an immune response is rare and consistent with similar incidences of known allergic responses to other legumes.

Based on the totality of the data and information, Nuritas concludes that fava bean protein hydrolysate is GRAS through scientific procedures under the conditions of its intended use.

### **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 fava bean protein hydrolysate 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 in NCE. OPMAS 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 Nuritas' notice concluding that fava bean protein hydrolysate 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 hydrolysate. Accordingly, our response should not be construed to be a statement that foods containing fava bean protein hydrolysate, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

## **Conclusions**

Based on the information that Nuritas provided, as well as other information available to FDA, we have no questions at this time regarding Nuritas' conclusion that fava bean protein hydrolysate is GRAS under its intended conditions of use. This letter is not an affirmation that fava bean protein hydrolysate 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 001166 is accessible to the public at [www.fda.gov/grasnoticeinventory](http://www.fda.gov/grasnoticeinventory).

Sincerely,

**Mical E.**

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for Susan J. Carlson, Ph.D.

Director

Division of Food Ingredients

Office of Pre-Market Additive Safety

Office of Food Chemical Safety, Dietary  
Supplements, and Innovation

Human Foods Program