



Nga Tran DrPH, MPH  
 Exponent, Inc.  
 1150 Connecticut Avenue, N.W., Suite 1100  
 Washington, DC 20036

Re: GRAS Notice No. GRN 000944

Dear Dr. Tran:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000944. We received the notice that you submitted on behalf of BASF Corporation (BASF) on May 29, 2020, and filed it on September 28, 2020. BASF submitted amendments to the notice on March 10, 2021, and April 2, 2021, providing additional information regarding the estimated dietary exposure, enzymes used during the manufacturing process, and analytical methods used to confirm the specifications.

The subject of the notice is enzyme-modified rice protein for use as a protein source in various foods at the maximum use levels specified in Table 1. The notice informs us of BASF’s view that this use of enzyme-modified rice protein is GRAS through scientific procedures.

Table 1. Food categories and corresponding maximum use levels of enzyme-modified rice protein.

<b>Foods</b>	<b>Maximum use level (weight %)</b>
Protein bars	50
Protein drink powders and squeezes	83
Breads, rolls	4.8
Cookies, other	10
Non-milk meal replacements	4.2
Breakfast cereals, ready-to-eat (RTE), weighing less than 20 g per cup	40
Breakfast cereals, RTE, weighing 20 g or more but less than 43 g per cup	15
Breakfast cereals, RTE, weighing not less than 43 g per cup	10
Soy milk	4.2
Vegetable and nut-based milks	4.2
Grain-based bars	20
Flavored milk drinks	1.04
Milk-based meal replacements	2.5
Yogurt	1.45
Frozen yogurt	2.0
Imitation meat products	1-64.3

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<b>Foods</b>	<b>Maximum use level (weight %)</b>
Fruit smoothies	20
Vegetable/tomato juice including vegetable smoothies	20
Soups, as consumed	0.96

Our use of the term, “enzyme-modified rice protein,” 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 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 “enzyme-modified rice protein.”

BASF provides information on the identity and composition of enzyme-modified rice protein. BASF describes enzyme-modified rice protein as a beige to light brown powder, prepared from whole-grain brown rice (*Oryza sativa*) through enzyme treatment. Enzyme-modified rice protein is composed primarily of protein (75-85%), with lesser amounts of fat (3-6%), dietary fiber (5-15%), and minerals, including sodium (1.4-1.9%), calcium (<0.5%), and potassium (<0.5%).

BASF describes the manufacturing process of enzyme-modified rice protein. First, the protein is extracted from food-grade whole-grain brown rice that has been cleaned, soaked in water, and treated with food-grade amylase to liquefy rice starch for removal. Second, the aqueous dispersion consisting of rice protein is pasteurized, cooled, and treated with a subtilisin enzyme preparation from *Bacillus amyloliquefaciens*<sup>1</sup> under controlled pH and temperature conditions for optimal enzymatic activity and to permit partial hydrolysis of the protein.<sup>2</sup> BASF states that subtilisin is inactivated by increasing the temperature to >80 °C, and the resulting product is subjected to drying (spray, drum or belt drying). The dried enzyme-modified rice protein is then sieved and packaged. BASF notes that enzyme-modified rice protein is manufactured using current good manufacturing practices and food-grade raw materials.

BASF provides specifications for the composition of enzyme-modified rice protein, expressed on a weight-percent basis, that include loss on drying (≤5%), protein content (≥75%), fiber (≤15%), and ash (≤7%). BASF also provides limits for pH (10% in water) of 7.5-9.0, total arsenic (≤0.2 mg/kg), cadmium (≤0.6 mg/kg), lead (≤0.4 mg/kg), mercury

<sup>1</sup> BASF states that the subtilisin enzyme preparation (EC 3.4.21.62) is produced using a non-toxicogenic and non-pathogenic *B. amyloliquefaciens*. BASF states that the enzyme meets the recommended purity specifications for food-grade enzymes established by the Joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA, 2006) and the Food Chemicals Codex (FCC, 2020).

<sup>2</sup> BASF notes that, based on the analyses for the degree of hydrolysis of the soluble portion of enzyme-modified rice protein, only a minor fraction of the total protein is hydrolyzed.

( $\leq 0.1$  mg/kg), mycotoxins, and microorganisms. BASF provides the results from the analyses of four non-consecutive lots to demonstrate that the enzyme-modified rice protein meets the stated specifications.

BASF states that the intended use of enzyme-modified rice protein is in part substitutional for the use of rice protein which is the subject of GRN 000609.<sup>3</sup> BASF provides a dietary exposure estimate to enzyme-modified rice protein from the intended uses using food consumption data from the 2013-2016 National Health and Nutrition Examination Surveys. Based on the maximum intended use levels of enzyme-modified rice protein, BASF estimates the eaters-only mean and 90<sup>th</sup> percentile dietary exposures for the U.S. population aged 2 years and older to be 10.3 and 23.4 g/person (p)/day (d), respectively. BASF also provides the eaters-only mean and 90<sup>th</sup> percentile cumulative dietary exposure to all rice protein ingredients to be 13.1 g/p/d and 25.2 g/p/d, respectively, for the U.S. population aged 2 years and older. BASF notes that these estimates are slightly above those resulting from the current uses of rice protein (mean of 12.3 g/p/d and 90<sup>th</sup> percentile of 22.2 g/p/d) as described in GRN 000609. BASF further notes that enzyme-modified rice protein is expected to replace existing sources of dietary plant-based protein and is not expected to increase the dietary exposure to total dietary protein. Based on the specification for total arsenic, BASF estimates the dietary exposure to total arsenic to be 0.08  $\mu\text{g}/\text{kg}$  body weight (bw)/d at the 90<sup>th</sup> percentile and notes that this estimate is below the Benchmark Dose Lower Confidence Limit (BMDL<sub>0.5</sub>) for inorganic arsenic established by JECFA (2011).

BASF incorporates all the safety information discussed in GRN 000609. BASF conducted an updated literature search for the safety information on rice protein or hydrolyzed rice protein published since GRN 000609 through April 2020 and notes that no new relevant safety studies were identified. BASF summarizes the published safety information discussed in GRN 000609, including studies which showed no adverse effects in oral toxicity studies in rats (acute studies) and mice (acute and mutagenicity studies). BASF addresses the allergenic potential of rice protein and discusses an unpublished allergenicity evaluation of enzyme-modified rice protein. BASF concludes that consumption of enzyme-modified rice protein is unlikely to result in allergic reactions. BASF observes that the incidence of food protein-induced enterocolitis syndrome associated with rice in the US is relatively uncommon.

BASF includes the statement of a panel of individuals (BASF's GRAS panel). Based on its review, BASF's GRAS panel concluded that enzyme-modified rice protein is safe under the conditions of its intended use.

Based on the data and information included in their notice, BASF concludes that enzyme-modified rice protein is GRAS for its intended use.

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<sup>3</sup> We responded to GRN 000609 (rice protein) and its supplement in letters dated June 6, 2016, and June 14, 2018, respectively, that we had no questions at that time regarding the notifier's GRAS conclusions.

## **Standards of Identity**

In the notice, BASF states its intention to use enzyme-modified rice protein 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 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 enzyme-modified rice protein 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 the Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety 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 BASF's notice concluding that enzyme-modified rice protein 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 enzyme-modified rice protein. Accordingly, our response should not be construed to be a statement that foods containing enzyme-modified rice protein, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

## **Conclusions**

Based on the information that BASF provided, as well as other information available to FDA, we have no questions at this time regarding BASF's conclusion that enzyme-modified rice protein is GRAS under its intended conditions of use. This letter is not an affirmation that enzyme-modified rice protein 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

000944 is accessible to the public at [www.fda.gov/grasnoticeinventory](http://www.fda.gov/grasnoticeinventory).

Sincerely,

Susan J. Carlson -S Digitally signed by Susan J.  
Carlson -S  
Date: 2021.10.08 16:10:15 -04'00'

Susan Carlson, Ph.D.  
Director  
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