



James La Marta, Ph.D.
Senior Manager, Regulatory Affairs
DSM Innovation Company
45 Waterview Boulevard
Parsippany, NJ 07054

Re: GRAS Notice No. GRN 000683

Dear Dr. La Marta:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000683. We received the notice you submitted on behalf of DSM Innovation Company (DSM) on December 19, 2016, and filed it on January 10, 2017. We received amendments to the notice on January 12, 2017, and March 13, 2017. These amendments provide clarification about confidential information,¹ determination of heavy metals, and potential allergenicity.

The subject of the notice is canola protein isolate (canola protein). The notice informs FDA of the view of DSM that canola protein is GRAS, through scientific procedures, for use as a source of protein, thickener, water binder, emulsifier, gelling agent, foaming agent, or texturizer in prepared foods (e.g., ready-to-eat meals, soups, pasta, snacks) at a maximum level of 10%, meat analogues at a maximum level of 30%, bakery products at a maximum level of 5%, protein-enriched bakery products at a maximum level of 30%, sports nutrition (e.g., protein drinks, energy bars) at a maximum level of 10%, meal replacement bars at a maximum level of 30%, beverages (e.g. fruit juices, soft drinks, juice blends) at a maximum level of 5%, dairy products at a maximum level of 5%, and medical and elderly nutrition products at a maximum level of 5%.

Our use of the term “canola 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

¹ GRN 000683 included information in the Appendices in Part 7 that was designated confidential in the notice we received on December 19, 2016. In the January 12, 2017, amendment, DSM states that contrary to the notation in Appendix 11, the allergen report, which was produced by a third party, DSM does not view any of the information contained in the GRAS notice to be confidential.

U.S. Food & Drug Administration
Center for Food Safety & Applied Nutrition
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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 “canola protein.”

DSM provides information about the identity and composition of canola protein. Canola protein is obtained from rapeseed press cake that is a byproduct of rapeseed oil production. The press cake used in the manufacture of canola protein is the crushed seeds of either *Brassica napus* or *Brassica juncea*. These varieties of rapeseed contain low levels of erucic acid and glucosinolates, and are also known as canola and used to produce oil for human consumption. DSM states that canola protein contains $\geq 90\%$ protein, which is approximately 40-65% cruciferins and 35-60% napins. Canola protein may also contain small amounts of moisture, fat, and carbohydrate from the rapeseed. Cruciferins are globulin proteins composed of 6 subunits with a total molecular weight of approximately 300 kDaltons (kDa). Napins are albumin storage proteins with a molecular weight of approximately 14 kDa.

DSM provides a description of the manufacturing method for canola protein. Rapeseed press cake is mixed with an aqueous salt solution and the insoluble material is removed by filtration or centrifugation. The pH of the remaining solution is adjusted with citric acid and ascorbic acid and the residual fat and precipitates are removed using a membrane filter press or centrifugation. The resulting solution is then concentrated and washed using an ultrafiltration and diafiltration step. The filtration step concentrates the protein and removes potential impurities, including polyphenols, phytate, and glucosinolates. DSM states that sodium bisulfite may be used to whiten the product.² The washed concentrate is then dried to obtain the final canola protein product. DSM states that all reagents and processing aids used in the manufacturing method are food grade and that canola protein is manufactured in accordance with current good manufacturing practices.

DSM provides specifications for canola protein that include a minimum content of total proteins ($\geq 90\%$ weight/weight (w/w)). Specifications also include limits for carbohydrates ($\leq 7\%$ w/w), fiber ($\leq 0.6\%$ w/w), fat ($\leq 2\%$ w/w), moisture ($\leq 7\%$ w/w), ash ($\leq 4\%$ w/w), lead (≤ 0.5 mg/kg), glucosinolates (≤ 1 micromol/g), phytates ($\leq 1.5\%$ w/w), and for microbial contaminants. DSM provides the results of five, non-consecutive batch analyses to demonstrate that canola protein meets the specifications.

DSM estimates the dietary exposure to canola protein based on the assumption that canola protein replaces all dietary protein and estimates of protein intake for the U.S. population using food consumption data from the National Health and Nutrition Examination Survey (NHANES 2011-2012). DSM estimates that the average protein intakes for adults are in the range of 80.0-102.9 g/d in men and 58.8-75.5 g/d in

² DSM states that canola protein produced using sodium bisulfite contains less than 10 mg/kg of residual sulfite.

women. Based on an estimated body weight (bw) of 60 kg for adults, the mean and 90th percentile protein intake is 1.6 and 3.2 g/kg bw/d for men and 1.1 and 2.2 g/kg bw/d for women, respectively. DSM estimates the mean and 90th percentile protein intake for children (2-19 years old) to be in the range of 57.8-95.1 g/d for boys and 53.3-63.2 g/d for girls. DSM states that the use of canola protein in food is self-limiting due to organoleptic factors and consumer taste considerations.

DSM discusses published and unpublished studies to support the safety of canola protein, noting its search of the literature through May 2016. DSM cites two published 13-week feeding studies in rats initially reported in GRN 000327 and states that they are the most relevant to demonstrate safety. DSM states that the purified canola protein isolates evaluated in these studies are similar to the canola protein product that is the subject of GRN 000683. In both of the 13-week feeding studies, rats were fed canola protein isolates at levels up to 20% of the diet. In the first study, cruciferin canola-rich protein isolate was fed at levels of 11.24 and 14.11 g/kg bw/d for males and females, respectively. In the second study, napin-rich canola protein isolate was fed at 12.46 and 14.95 g/kg bw/d for males and females, respectively. DSM notes that neither study demonstrated any toxicological adverse effects.

Additionally, DSM cites an unpublished genotoxicity report initially discussed in GRN 000327. The report states that cruciferin and napin protein isolates were evaluated using the reverse mutation assay (Ames assay), mouse micronucleus, and mouse lymphoma tests. Neither of the canola protein isolates was found to be mutagenic or clastogenic. Finally, DSM requested the Food Allergy Research and Resource Program at the University of Nebraska to compare the potential allergenicity of canola protein to the eight major food allergens. DSM states that their canola protein product would be unlikely to cause an allergic reaction.

DSM includes the statement of a panel of individuals (DSM's GRAS panel). Based on its review, DSM's GRAS panel concluded that canola protein is safe under the conditions of its intended use.

Based on the data and information described above, DSM concludes that canola protein is GRAS for its intended use in food.

Standards of Identity

In the notice, DSM states its intention to use canola protein 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

In describing one of the intended uses of canola protein as a source of protein, DSM lists meal replacements and nutritional bars, two food categories that often contain health or

nutrient content claims. 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). The notice raises a potential issue under these labeling provisions. In the notice, DSM states that canola protein will be used as a source of protein. If products containing canola 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. 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 its review of DSM's notice that canola protein is GRAS for the intended use, FDA did not consider whether section 301(ll) or any of its exemptions apply to foods containing canola protein. Accordingly, this response should not be construed to be a statement that foods that contain canola protein, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that DSM provided, as well as other information available to FDA, we have no questions at this time regarding DSM's conclusion that canola protein is GRAS under its intended conditions of use. This letter is not an affirmation that canola 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 000683 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,
**Michael A.
Adams -S**
Dennis M. Keefe, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

Digitally signed by Michael A. Adams -S
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