Justyna Pałasińska
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Re: GRAS Notice No. GRN 001122

Dear Ms. Pałasińska:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001122. We received the notice that you submitted on behalf of NapiFeryn BioTech Sp. z o. o. (NapiFeryn) on September 23, 2022, and filed it on April 19, 2023.[1] NapiFeryn submitted amendments to the notice on July 11, 2023, July 17, 2023, August 28, 2023, October 19, 2023, October 31, 2023, and July 3, 2024 providing clarifying information regarding the intended uses, specifications, suitability data, safety information, and correcting clerical errors.

The subject of the notice is canola concentrate for use at the maximum use levels specified in Table 1 as an ingredient, source of protein, formulation aid, stabilizer, thickener, or texturizer in various foods and as a binder and extender in processed meat and poultry.[2] The notice informs us of NapiFeryn's view that these uses of canola concentrate are GRAS through scientific procedures.

Table 1. Food uses of canola concentrate and corresponding maximum use levels

Food uses	**Maximum use level (%)**
Bakery products and baking mixes	20
Non-alcoholic beverages and beverage bases (fruit and/or vegetable drinks, smoothies, "energy" drinks)	7
Coffee and tea (including instant)	7
Breakfast cereals	35
Grain products, pastas	20
Milk products and dairy alternatives	15
Egg substitutes and egg products alternatives	7

[1] The contact person for GRN 001122 was updated in a correspondence dated December 4, 2023.
[2] NapiFeryn states that canola concentrate is not intended for use in infant formula.

Fat, oils, and salad dressings	10
Meat product alternatives	20
Processed meat and poultry	15
Fruit and water ices	7
Batters and breadings	10
Spices and seasoning mixes	5
Protein-fiber and nutritional powders	100
Nutritional and protein bars	20
Nut products	30
Processed fruits, vegetables, and legumes	30
Sauces, dips, gravies, and condiments	10
Snack foods	40
Soup and soup mixes	15
Confections, candies, and frostings	20
Jams, jellies, gelatins, puddings, fillings	30
Sweet sauces, toppings, and syrups	10

Our use of the term, "canola concentrate," 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 (CFSAN). The Office of Food Additive Safety (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "canola concentrate."

NapiFeryn describes canola concentrate as a white to off-white powder obtained from the rapeseed press cake that is a byproduct of rapeseed (canola) oil production. The press cake used in the manufacture of canola concentrate is the crushed seed of *Brassica napus* and/or *B. juncea* and/or *B. rapa*.[3] NapiFeryn states that canola concentrate contains 30-45% protein and 40-70% fiber.[4]

NapiFeryn describes the manufacturing process for canola concentrate that begins with an aqueous extraction of cold-pressed rapeseed cake to yield a residual slurry. The pH of the slurry is optionally adjusted with hydrochloric acid to enhance removal of anti-

[3] NapiFeryn states that rapeseed press cake is sourced solely from low-erucic acid rapeseed varieties.
[4] The definition of "dietary fiber" in 21 CFR 101.9(c)(6)(i) was added by FDA's final rule revising the nutrition and supplement facts labels (81 FR 33742, May 27, 2016). This final rule, among other things, defines dietary fiber as non-digestible soluble and insoluble carbohydrates (with three or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with three or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health. Questions related to whether canola concentrate would meet the regulatory definition of "dietary fiber" should be directed to ONFL.

nutritional factors. The slurry is then subjected to centrifugation or a filter press to remove the excess liquid. The separated solids are washed with 40-95% (w/w) ethanol and ethyl acetate to further reduce levels of anti-nutritional factors, fats, and lipids. The solids are then separated from the solution and dried to obtain canola concentrate. NapiFeryn states that if the rapeseed press cake used in the manufacturing process contains hulls, a suitable separation step is employed to remove residues of the hull fraction from the final canola concentrate. NapiFeryn states that canola concentrate is manufactured according to current good manufacturing practices using food grade raw materials and processing aids that are authorized for use in food manufacture in the U.S.

NapiFeryn provides specifications for canola concentrate that include protein (30-45%), total carbohydrates (≤70% by difference), fat (≤2%), ash (≤5%), moisture (≤7%), glucosinolates (≤0.3 mmol/kg), phytates (≤2%), lead (≤0.35 mg/kg), mercury (≤0.1 mg/kg), arsenic (≤0.15 mg/kg), cadmium (≤0.1 mg/kg), ethanol (<200 mg/kg), ethyl acetate (<200 mg/kg), sulphur dioxide (<10 mg/kg), and limits for microorganisms. NapiFeryn provides the results from the analyses of five non-consecutive batches to demonstrate that canola concentrate can be manufactured to meet these specifications. NapiFeryn states that canola concentrate is stable for at least 24 weeks at 25 °C and 60% relative humidity.

NapiFeryn estimates the dietary exposure to canola concentrate from the intended uses using food consumption data from the 2017-2018 National Health and Nutrition Examination Survey. NapiFeryn estimates the eaters-only dietary exposure to canola concentrate to be 19.3 g/person (p)/d (0.28 g/kg body weight (bw)/d) at the mean and 40.8 g/p/d (0.59 g/kg bw/d) at the 90th percentile for the U.S. population aged 2 years and older. NapiFeryn states that the intended uses of canola concentrate will be substitutional for other protein and fiber sources and therefore, there is not expected to be any additional dietary exposure to protein and fiber.

NapiFeryn discusses relevant, publicly available safety data and information for canola concentrate, inclusive of studies on other rapeseed products, and cites previous GRAS conclusions from GRNs 000327, 000386, and 000683.[5] NapiFeryn performed a literature search and notes that no additional data was found that would contradict the current GRAS conclusion. NapiFeryn reports that canola concentrate is non-mutagenic and non-genotoxic based on *in vitro* genetic toxicity assays using defatted rapeseed powder, which NapiFeryn concludes is compositionally similar to canola concentrate based on their analytical data. Additionally, NapiFeryn provides analytical data on anti-nutritional factors in canola concentrate, including erucic acid, phenolics, phytic acid, glucosinolates, and trypsin inhibitors, and concludes that the levels of these anti-nutritional components are comparable to other rapeseed products that are concluded to be GRAS for their intended uses.

[5] The subjects of GRNs 000327, 000386, and 000683 are cruciferin-rich and napin-rich canola/rapeseed protein isolates, hydrolyzed canola protein isolate, and canola protein isolate, respectively. FDA evaluated these notices and responded in letters dated August 23, 2010, December 28, 2011, and May 10, 2017, stating that we had no questions at that time regarding the respective notifiers' GRAS conclusions.

NapiFeryn cites two published 13-week feeding studies in rats initially reported in GRN 000327 and discuss their relevance to demonstrate safety of canola concentrate. NapiFeryn concludes that the purified canola protein isolates evaluated in these studies are similar to canola concentrate, which is primarily composed of the proteins cruciferin and napin. In the 13-week feeding studies, rats were fed either cruciferin- or napin-rich canola protein isolate at levels up to 20% of the diet. NapiFeryn reports that the only adverse effect noted in these studies was an increase in thyroid weight at the highest dose tested. Noting that this observation was made without accompanying histopathological changes, NapiFeryn conclude this finding was not toxicologically relevant. NapiFeryn further suggests that this observation may be due to the high level of glucosinolates in the test articles used and thus not relevant to the safety of their article of commerce. In support of their contention, NapiFeryn notes that the raw material used for the production of canola concentrate is low in glucosinolates, and that the manufacturing of canola concentrate minimizes the presence of glucosinolates in the final product. Given the analytical data provided by NapiFeryn demonstrates total glucosinolates are not detected in the final product, consumer exposure to dietary glucosinolates through canola concentrate at the intended use level is expected to be negligible. Additionally, NepiFeryn discusses a European Food Safety Authority (EFSA) conclusion on partially defatted rapeseed powder, which is supportive of the current GRAS conclusion.

NapiFeryn discusses published data on rapeseed protein allergenicity and its cross-reactivity with white mustard and other *Brassicaceae*, like the turnip rape, and concludes that canola concentrate would not be expected to cause an allergic reaction except for in those individuals allergic to mustard or other plants in the *Brassicaceae* family because it contains similar proteins. NapiFeryn discusses the safety of protein and fiber consumption in general, and notes that dietary exposure to protein or fiber from canola concentrate under its intended conditions of use does not exceed the Institute of Medicine's Recommended Dietary Allowance for protein or Adequate Intake for fiber.

Based on the available data and information, NapiFeryn concludes that canola concentrate is GRAS for its intended uses.

Standards of Identity

In the notice, NapiFeryn states its intention to use canola concentrate 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 canola concentrate 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 CFSAN. 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.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 001122, we coordinated with the Food Safety and Inspection Service (FSIS) of the United States Department of Agriculture. Under the Federal Meat Inspection Act, the Poultry Products Inspection Act, and the Egg Products Inspection Act, FSIS determines the efficacy and suitability of ingredients used in meat, poultry, and egg products, and prescribes safe conditions of use. Suitability relates to the ingredient's effectiveness in performing its intended technical effect and the assurance that the ingredient's use will not result in products that are adulterated or misleading for consumers.

FSIS has advised the following with respect to the statutes it administers:

> FSIS completed its review and has no objection to the use of canola concentrate as a binder and extender in FSIS-regulated meat and poultry products at levels of up to 15%, where standards of identity permit such use and provided the substance is applied in accordance with manufacturers specifications in a manner that dust/airborne particles are mitigated when canola concentrate is incorporated into product formulations.
>
> Regarding labeling, meat and poultry products containing canola concentrate are required to be labeled in the ingredients statement with the common or usual name. Based on this substance's composition (30-45% protein, 40-70% fiber (dry matter basis), and less than 2% oil), the common or usual name for this product is "isolated canola product."

FSIS requested that we advise you to seek regulatory guidance from its Risk Management and Innovations Staff (RMIS) about the use of canola concentrate in meat, poultry, and egg products. You should direct such an inquiry to Stephanie Hretz, Director, RMIS, Office of Policy and Program Development, FSIS by email at Stephanie.Hretz@usda.gov.

Section 301(ll) of the Federal Food, Drug, and Cosmetic 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 NapiFeryn's notice concluding that canola concentrate 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 canola concentrate. Accordingly, our response should not be construed to be a statement that foods containing canola concentrate, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that NapiFeryn provided, as well as other information available to FDA, we have no questions at this time regarding NapiFeryn's conclusion that canola concentrate is GRAS under its intended conditions of use. This letter is not an affirmation that canola concentrate 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 001122 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

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Director
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cc: Stephanie Hretz, M.P.H.
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