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April 18, 2006

## **BY FEDEX**

Division of Docket Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

**Re: Comments to Docket No. 2006D-0066 - Guidance for Industry and  
FDA Staff: Whole Grains Label Statements**

Dear Sir or Madam:

We write to you on behalf of our client, Pizzey Milling ("Pizzey"), a manufacturer of flaxseed supplements, to submit comments to Docket Number 2006D-0066, Guidance for Industry and FDA Staff: Whole Grains Label Statements ("Draft Guidance").

We understand that the Draft Guidance is intended to provide guidance to industry regarding what the agency considers to be "whole grain" and assist manufacturers in labeling their products accordingly. The Draft Guidance states that cereal grains that consist of intact, ground, cracked or flaked caryopsis whose principal anatomical components - the starchy endosperm, germ and bran - are present in the same relative proportion as they exist in the intact caryopsis - should be considered whole grain foods. The Draft Guidance lists amaranth, barley, buckwheat, bulgur, corn (including popcorn), millet, quinoa, rice, rye, oats, sorghum, teff, triticale, wheat and wild rice as examples of cereal grains that should be considered whole grain foods. The Draft Guidance also indicates that products derived from legumes, oilseeds (sunflower seeds), and roots (e.g., arrowroot) should not be considered whole grain foods. Thus, the Draft Guidance excludes products derived from flaxseed, an oilseed, from the category of whole grain foods.<sup>1</sup>

<sup>1</sup> Notably, the Draft Guidance uses the terms "cereal grains" and "oilseeds" without defining these terms. The standard definition of an oilseed is defined by the use: "a seed or crop mainly grown for oil." See Merriam Webster Online Dictionary (www.m-w.com). Although flaxseed was traditionally used for oil by the oilseed crushing industry, within the past ten years there has been a significant shift toward using flaxseed as a whole seed for nutraceutical products. An oilseed that has similar nutrient content as a cereal grain when the whole grain is

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Excluding products derived from flaxseed from the category of whole grain foods simply because flaxseed is an oilseed does not make sense because flaxseed has many of the same essential nutrients and health benefits as the cereal grains listed in the Draft Guidance. As set forth below, flaxseed has more dietary fiber than many of the cereal grains included as whole grain foods; is a good source of phytonutrients; and is high in essential fatty acids. As a result, flaxseed has also been found to have beneficial effects with regard to cardiovascular disease, as set forth in more detail below. Accordingly, we strongly encourage the FDA to revise the Draft Guidance by deleting the reference to products derived from "oilseeds" as a category of foods that should not be considered whole grain foods. In addition, we strongly encourage the FDA to add flaxseed as an example of a food that should be considered a whole grain food when the starchy endosperm, germ and bran are present in the same relative proportion as they exist in the intact caryopsis.

#### **I. Whole Grain Flaxseed is High in Several Essential Nutrients**

It is widely recognized that Whole Grain foods have numerous potential health benefits, including with regard to cardiovascular heart disease, obesity and cancer. The health benefit are attributable to large concentrations of several key nutrients, including fiber and phytonutrients. However, it is believed that the whole grain is greater than the sum of it's parts, as there is a synergistic effect from these ingredients. It has been noted that "[a]lthough it is difficult to separate the protective properties of whole grains from dietary fibre and other components, the disease protection seen from whole grains in prospective epidemiological studies far exceeds the protection from isolated nutrients and phytochemicals in whole grains."<sup>2</sup> Any whole grain food which contains these key ingredients should be considered a whole grain food, regardless of whether the source is a cereal grain or an oilseed such as flaxseed.

As with cereal grains, whole grain products derived from flaxseed are a good source of both dietary fiber and phytonutrients, which together are believed to be largely responsible for the health benefits of whole grains. Unlike some cereal grains, whole grain products derived from flaxseed are also a good source of essential fatty acids (including both ALA and LA) and protein. An analysis of brown Canadian flax averaged 41% fat, 20% protein, 28% total dietary fiber, 7.7% moisture and 3.4% ash, which is the mineral-rich residue left after samples are burned<sup>3</sup>. Additional nutrient details are set forth in detail in Exhibit A, which compares the nutrient content of flaxseed to two "cereal grains" listed in the FDA draft guidance, namely wheat, corn, as well as soybeans.

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consumed should not be excluded from whole grain claims merely because the traditional use of the product was as for oil.

<sup>2</sup> Slavin, J. 2004. Whole grains and human health. *Nutr Research Rev*; 17, 99-110. This article provides a good overview of the known relationship between whole grains and human health by describing the roll of the key nutrients found in whole grains, which are also found in whole grain flaxseed.

<sup>3</sup> Morris, DH, *Flax A Health and Nutrition Primer* 3<sup>rd</sup> Edition, Flax Council of Canada, page 11.

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**A. Whole Grain Flaxseed is High in Dietary Fiber**

Like many of the cereal grains listed by way of example as whole grain foods, whole flax seeds and ground flax are excellent sources of dietary fiber. Total fiber accounts for about 28% of the weight of full-fat flax seeds, with a ratio of soluble to insoluble fiber between 20:80 and 40:60<sup>4</sup>. The American Dietetic Association has cited the "significant impact" that fiber can have on the prevention of obesity, cardiovascular disease and type 2 diabetes<sup>5</sup>. The primary action of fiber in the body is in the gastrointestinal tract, but not all fiber sources have the same physiological effects. Generally, concentrates of water-soluble fibers delay transit through the stomach and small intestine<sup>6</sup>. Soluble fibers are rapidly broken down (fermented) by bacteria in the large intestine and do not promote laxation. Fibers that are predominantly water insoluble promote laxation and are either slowly or not fermented<sup>7</sup>.

Insoluble dietary fiber also plays an important role in the relief of constipation, a common problem among many individuals who consume low fiber diets, are inactive, or are using certain medications for other conditions that may promote constipation as a side effect. Diets high in insoluble fiber result in good colon health, which may have protective effects against colon cancer. Correlation studies that compared colorectal cancer incidence or mortality rates among countries with estimates of national dietary fiber consumption suggest that fiber intake may be protective against colon cancer<sup>8</sup>. When results of 13 case-control studies of colorectal cancer rates and dietary practices were pooled, it was concluded that the results provided substantive evidence that intake of fiber-rich foods is inversely related to risks of both colon and rectal cancer<sup>9</sup>.

In addition, diets high in dietary fiber, both soluble and insoluble types, have demonstrated beneficial effects on weight loss. Studies have shown that high fiber foods, such as flax, deliver more bulk in the diet with less energy, which in turn may influence satiety as well as alter certain hormone responses such as cholecystokinin and insulin<sup>10</sup>.

In fact, when the National Academy of Sciences/Institute of Medicine recently published their report on the Dietary Reference Intakes for Macronutrients, the dietary requirement for fiber was increased significantly based on scientific evidence of its health

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<sup>4</sup> Hadley, M., Lacher, C., Mitchell-Fetch, J. 1992. Fiber in Flaxseed. *Proc. Flax Inst*; 54: 79-83.

<sup>5</sup> American Dietetic Association. 1997. Health implications of dietary fiber -- Position of ADA. *J Am Diet Assoc*; 97:1157-1159.

<sup>6</sup> Wolever TMS, Jenkins DJA. 1993. Effect of dietary fiber and foods on carbohydrate metabolism. In: Spiller GA, ed. *CRC Handbook of Dietary Fiber in Human Nutrition*. 2nd ed. Boca Raton, Fla: CRC Press; 111-152.

<sup>7</sup> *Physiological Effects and Health Consequences of Dietary Fiber*. Bethesda, Md: Life Sciences Research Office, Federation of American Societies for Experimental Biology; 1987.

<sup>8</sup> Bingham SA. 1990. Mechanisms and experimental and epidemiological evidence relating dietary fiber (nonstarch polysaccharides) and starch to protection against large bowel cancer. *Proc Nutr Soc*; 49:153-171.

<sup>9</sup> Howe GR, Benito E, Castelleto R, et al. 1992. Dietary intake of fiber and decreased risk of cancers of the colon and rectum: evidence from the combined analysis of 13 case-control studies. *J Natl Cancer Ins*; 84:1887-1896.

<sup>10</sup> Anderson, J.W. and Bryant, C.A. 1986. Dietary fiber: Diabetes and obesity. *Am. J. Gastroenterol*; 81: 898-906.

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benefits. At the recent Whole Grains & Health. A Global Summit conference on May 20, 2005, in Minneapolis, Minnesota, Dr. Lester M. Crawford, D.V.M., PH.D., acting Commissioner of Food and Drugs, stated that:

“Many of you may know that when the National Academy of Sciences/Institute of Medicine published their report on the Dietary Reference Intakes for Macronutrients, the dietary requirement for fiber was increased significantly based on scientific evidence of its health benefits. The requirement was set at 14 grams of fiber per 1000 calories. So the average person with a 2000-calorie intake needs 28 grams of fiber per day. It’s extremely difficult to get that much fiber in your diet without the consumption of whole grains, and the Dietary Guidelines recognize and promote the intake of whole grains as an important source of dietary fiber.”

Whole grain flaxseed can be used to help individuals reach the recommended levels of dietary fiber. The chart attached as Exhibit A compares the nutrient content of four different types of foods, two of which (wheat and corn) are currently included as whole grain foods in the Draft Guidance. Notably, whole grain flaxseed has 2.2 times the dietary fiber per 100 grams as wheat, and 3.7 times the fiber per 100 grams as corn, which are both listed as examples of whole grain foods in the Draft Guidance.

**B. Whole Grain Flaxseed is A Good Source of Phytonutrients**

There is also evidence that plant lignans and other phytonutrients found in whole grains play an important role in the prevention of CHD. Plant lignans are phenolic compounds formed from the coupling of two cinnamyl alcohols. They are biologically active phytochemicals that act in the body as antioxidants, which are natural compounds that help reduce the risk of many types of cancer, such as breast, colon and prostate cancer. Oilseeds, particularly flaxseed, produce the highest concentration of lignans.<sup>11</sup> Again, although it is difficult to separate the protective properties of the various nutrients in whole grains, “the disease protection seen from whole grains in prospective epidemiological studies far exceeds the protection from isolated nutrients and phytochemicals in whole grains.”<sup>12</sup>

**C. Whole Grain Flaxseed Is High In Essential Fatty Acids**

In addition to containing the same type of nutrients found in whole grain cereal grains, Flax is also rich in essential fatty acids, which have been found to provide additional health benefits and are lacking in the diet of the typical American. Whole grain flaxseed contains a mixture of fatty acids, but it is rich in polyunsaturated fatty acids, particularly alpha-

<sup>11</sup> Nesbitt PD, Lam Y, Thompson LU. 1999. Human metabolism of mammalian lignan precursors in raw and processed flaxseed. *Am. J. Clin. Nutr.* 69: 549-55.

<sup>12</sup> Slavin, J. 2004. Whole grains and human health. *Nutr Research Rev;* 17, 99.

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linolenic acid (ALA or LNA, as it is sometimes abbreviated), the essential omega-3 fatty acid, and linoleic acid (LA), the essential omega-6 fatty acid. *See* Exhibit A. ALA constitutes 57% of the total fatty acids in flax, making flax the richest source of ALA in the North American diet<sup>13</sup>. Linoleic acid constitutes 16% of total fatty acids<sup>14</sup>. Flaxseed has a low level of the nutritionally undesirable saturated fatty acids, which constitute 9% of total fatty acids.<sup>15</sup> The level of the desirable monounsaturates in flaxseed is modest (18%).<sup>16</sup>

Essential fatty acids (EFAs) are required in the diet as they can not be synthesized by humans from the shorter chain fatty acid, oleic acid (C18:1). The two established EFAs are 1) linoleic acid (C18:2, LA), which is converted in the body into longer chain omega-6 fatty acids; and 2) ALA, which is converted in the body into longer chain omega-3 fatty acids. LA and ALA are components of cellular membranes and act to increase membrane fluidity. These fatty acids are necessary for cell membrane function, as well as for the proper functioning of the brain and nervous system.

Omega-3 fatty acids may also reduce the risk of cardiovascular heart disease (CHD), as the Office of Management and Budget recently recognized in a letter to the Department of Health and Human Services.<sup>17</sup> In this letter the OMB urged the Department of Health and Human Services to revise the nation's dietary guidelines to include information that omega-3 fatty acids may reduce the risk of CHD. The OMB based this recommendation on the growing body of scientific evidence that find an increase in the consumption of omega-3 fatty acids results in reduced deaths due to CHD. The FDA has also recognized the potential health benefits of omega-3 fatty acids and has approved a qualified health claim for reduced risk of coronary heart disease (CHD) on conventional foods that contain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) omega-3 fatty acids.

Thus, in addition to having similar or higher levels of fiber and plant lignans, whole grain flaxseed also provides the additional benefit of being a source of omega-3 fatty acids, which may also reduce the risk of CHD. Notably, flaxseed is the only whole grain which is also a good source of omega-3 fatty acids. This makes flaxseed the best low cost alternative to other sources of omega-3 fatty acids, such as fish and fish oils, which tend to be very expensive.

#### **D. Whole Grain Flaxseed Is A Good Source Of Protein and Low in Carbohydrates**

Whole Grain Flaxseed is also a good source of protein, with more protein per 100 grams (g) (18.29 g) than either wheat (13.68 g) or corn (9.42), and is low in carbohydrates

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<sup>13</sup> Daun JK, Barthelet VJ, Chornick TL, Duguid S. 2003. Structure, composition, and variety development of flaxseed. In: *Flaxseed in Human Nutrition*, 2<sup>nd</sup> ed. Thompson LU, Cunnane SC, eds. Champaign: AOCS Press: 1-40.

<sup>14</sup> *Id.*

<sup>15</sup> *Id.*

<sup>16</sup> *Id.*

<sup>17</sup> Letter from John D. Graham, May 27, 2003, Office of Management and Budget, attached as Exhibit B.

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(sugars and starches), providing only 28.88 grams (g) per 100g. *See Exhibit A.* Whole grain flaxseed is also higher in calcium, potassium and magnesium than wheat or corn, and has comparable levels of iron and zinc. *See Exhibit A.*

Flaxseed is also gluten-free. Gluten is a protein found in many of the cereal grains listed in the Draft Guidance, including wheat, oats, barley and rye. The specific agent in gluten that causes the condition known as gluten enteropathy (also known as gluten intolerance or celiac disease) is gliadin, which is rich in the amino acids proline and glutamine. Although the mechanism by which dietary gluten irritates the mucosal lining of the gastrointestinal tract in susceptible people is not well understood, and an estimated 1 in 133 Americans suffer from this condition.<sup>18</sup> For these people in particular, Whole Grain Flaxseed could provide a good alternative to cereal grains with gluten, thereby helping these individuals increase the amount of whole grain foods in their diet.

In sum, the composition of Flaxseed in terms of essential nutrients compares favorably with the composition of the cereal grains listed by the FDA as whole grain foods, including corn and wheat, as demonstrated by the chart attached as Exhibit A. The composition of flaxseed is superior to corn, another oilseed that is listed as a whole grain food by the FDA, with respect to almost every essential nutrient.

## II. Flaxseed Has Been shown to Have Cardiovascular Health Benefits

Flaxseed has been shown to have significant benefits with regard to cardiovascular heart disease (CHD). The consumption of 2-6 tbsp of ground flax daily for four weeks reduced blood total and LDL cholesterol significantly in clinical trials. Blood total cholesterol decreased 6-9% and LDL cholesterol decreased 9-18% in studies of healthy young adults<sup>19</sup>, men and women with moderately high levels of blood cholesterol<sup>20</sup> and postmenopausal women<sup>21</sup> who ate ground flax. High-density lipoprotein (HDL) cholesterol and triglyceride levels were not affected. The effect of ground flax on blood lipids was confounded in these studies by the fiber content of flax.

In another study, Jenkins and colleagues proposed that the mucilage gums are most likely responsible for the lipid-lowering effects of flax<sup>22</sup>. In their study, 29 men and

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<sup>18</sup> Alessio Fasano, MD, et. al., *Arch Intern Med.* 2003;163:286-292.

<sup>19</sup> Cunnane SC, Ganguli S, Menard C, et al. 1993. High  $\alpha$ -linolenic acid flaxseed (*Linum usitatissimum*): Some nutritional properties in humans. *Br. J. Nutr.*; 69: 443-453; Cunnane SC, Hamadeh MJ, Liede AC, et al. 1995. Nutritional attributes of traditional flaxseed in healthy young adults. *Am. J. Clin. Nutr.*; 61: 62-68

<sup>20</sup> Bierenbaum ML, Reichstein R, Watkins TR. 1993. Reducing atherogenic risk in hyperlipemic humans with flax seed supplementation: A preliminary report. *J. Am. Coll. Nutr.*; 12: 501-504.

<sup>21</sup> Lucas EA, Wild RD, Hammond LJ, et al. 2002. Flaxseed improves lipid profile without altering biomarkers of bone metabolism in postmenopausal women. *J. Clin. Endocrinol. Metab.*; 87: 1527-1532.

<sup>22</sup> Jenkins DJA, Kendall CWC, Vidgen E, et al. 1999. Health aspects of partially defatted flaxseed, including effects on serum lipids, oxidative measures, and ex vivo androgen and progestin activity: A controlled crossover trial. *Am. J. Clin. Nutr.*; 69: 395-402.

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women with high blood cholesterol levels ate muffins made with wheat bran or muffins made with partially defatted flax for three weeks. The subjects ate four muffins daily, which provided 50 g of partially defatted flax. Partially defatted flax contains less than 10% fat by weight, whereas regular flax contains about 41% fat. The subjects' total cholesterol decreased about 5% and LDL cholesterol decreased 8% on the partially defatted flax diet.

In yet another study, the lipid lowering effects of whole flaxseed versus sunflower seed in 38 postmenopausal women were investigated in a double blind, randomized, crossover trial. Subjects consumed 38g of whole flaxseed or whole sunflower seed incorporated into bread or muffins for a six-week period<sup>23</sup>. Following a 2-week washout period, participants resumed treatment for an additional six-week period. LDL cholesterol decreased by 14.7% in the flax group in comparison to the sunflower seed group. No effects on triglyceride or HDL levels were observed in either group. This study in particular demonstrates why sunflower seed and flaxseed should not be lumped together as oilseeds in the draft guidance.

In sum, unlike some other oilseeds, whole grain flaxseed has been found to help reduce total cholesterol and LDL levels (bad cholesterol), which contributes to a healthy cardiovascular system. These cardiovascular health benefits are similar to the health benefits found for products derived from some of the other cereal grains included in the draft guidance as whole grain foods. Accordingly, products derived from flaxseed should also be included as whole grain foods.

### III. Conclusion

Making an general distinction between cereal grains and oilseeds is an overly simplistic approach to determining what foods should be considered whole grain foods. Flaxseed is one oilseed that is comparable with or superior to the cereal grains listed by the FDA in terms of essential nutrients, including dietary fiber, essential fatty acids and phytonutrients. Studies have also has shown that whole grain flaxseed has cardiovascular health benefits by leading to a reduction in total cholesterol and LDL levels. Accordingly, we strongly encourage the FDA to revise the Draft Guidance to delete the general reference to "oilseeds" from the list of foods that should not be considered whole grains.<sup>24</sup> In addition, Pizzey believes that the FDA should include flaxseed as an example of a product that should be considered a whole grain product if the flaxseed product consists of intact, ground, cracked or flaked caryopsis whose principal anatomical components are present in the same relative proportion as they exist in the intact caryopsis.

We appreciated your consideration of these comments and hope that the FDA will entertain the proposed revisions to the Draft Guidance. Whole grain foods are an important and

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<sup>23</sup> Arjmandi, B.H., Khan, D.A., Juma, S., et al. 1998. Whole flaxseed consumption lowers serum LDL-cholesterol and lipoprotein (a) concentrations in postmenopausal women. *Nutr Res*; 18: 1203-1214.

<sup>24</sup> Pizzey does not object to the inclusion of products derived from sunflower seeds as food products that should not be considered whole grain foods, but only to the inclusion of the general category of oilseeds. Unlike the hull of flaxseed, the hull of a sunflower seed is inedible.

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undervalued food in the American diet, and whole grain flaxseed can be an important contributor towards increasing the consumption of whole grains if products that contain whole grain flaxseed are permitted to advertise this fact.

If you have any questions or would like additional information related to these comments, please contact me at 312-558-8024, or by email at [bfergemann@winston.com](mailto:bfergemann@winston.com).

Respectfully submitted,

A handwritten signature in black ink, appearing to read "B. Fergemann", written over a horizontal line.

Brian D. Fergemann, Esq.

BF:bdf

cc: Linda Pizzey (Pizzey's Milling)  
Stephen P. Durchslag, Esq.