

PETITION FOR AMENDED HEALTH CLAIM ^{P1 55}
FOR
FOODS AND DIETARY SUPPLEMENTS:

“CONSUMPTION OF OMEGA-3 FATTY ACIDS MAY REDUCE THE RISK OF
CORONARY HEART DISEASE.”

SUBMITTED TO THE FOOD AND DRUG ADMINISTRATION
JUNE 23, 2003

0868 '03 JUN 23 P2:10

PETITIONERS:

WELLNESS LIFESTYLES, INC. D/B/A AMERICAN LONGEVITY
AND
LIFE EXTENSION FOUNDATION BUYERS CLUB, INC.

2003 Q-0401

QHC 1
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BACKGROUND OF THE PETITIONERS

Incorporated in the state of California, Wellness Lifestyles, Inc. (d/b/a American Longevity) manufactures, distributes, and sells dietary supplements, including omega-3 fatty acids-containing dietary supplements.

The Life Extension Foundation Buyers Club, Inc. was officially incorporated in 1980, but the founders have been involved in anti-aging research since the 1960s. Life Extension is engaged in the business of manufacturing, marketing, distributing, and selling over 400 pharmaceutical grade dietary supplements, including omega-3 fatty acids-containing dietary supplements.

June 23, 2003

PETITIONERS: Wellness Lifestyles, Inc. and Life Extension Foundation Buyers Club, Inc.
ADDRESS: c/o Emord & Associates, P.C.
5282 Lyngate Court
Burke, VA 22015
SUBJECT: Petition for Amended Health Claim: Omega-3 Fatty Acids and Coronary Heart Disease

Food and Drug Administration
Office of Nutritional Products, Labeling, and Dietary Supplements
HFS-800
5100 Paint Branch Parkway
College Park, MD 20740

Introduction and Statement of Purpose

The undersigned, Wellness Lifestyles, Inc. and Life Extension Foundation Buyers Club, Inc. (hereinafter "Petitioners"), submit this petition pursuant to Sections 403(r)(3) and (r)(5)(D) of the Federal Food, Drug and Cosmetic Act ("FDCA") (21 U.S.C. §§ 343(r)(3) and (r)(5)(D)) with respect to the relationship between the consumption of omega-3 fatty acids¹ and coronary heart disease risk reduction. Specifically, the Petitioners request that the disclaimer on the current omega-3 fatty acids/coronary heart disease dietary supplement health claim be removed and that the claim be extended to omega-3 containing foods. The amended claim is contained in section V below. Attached hereto, and constituting a part of this petition, are all of the items specified in 21 C.F.R. § 101.70(f).

This petition presents a logical and valid evaluation of the scientific studies and clinical trials published since FDA allowed a revised version of the claim,² first submitted to FDA by Julian M. Whitaker, M.D., et al. in their November 22, 1999 Comments to FDA (Docket No.

¹ A used herein, omega-3 fatty acids refers to a group of polyunsaturated fatty acids ("LCPUFA") comprised of eicosapentaenoic acid ("EPA"), docosahexaenoic acid ("DHA"). See Exhibit 1 at 145.

² FDA granted the revised claim in a letter from Christine J. Taylor, Ph.D. dated February 8, 2002.

91N-0103), concerning omega-3 fatty acid's effect on reduction in the risk of coronary heart disease.³ Omega-3 fatty acids are lipids found in fish and other marine life such as phytoplankton. See PDR for Nutritional Supplements (2001) at 145 (Attached as Exhibit 1). They are known to have anti-arrhythmic and anti-inflammatory properties. See id. at 146; see also Exhibit 2 at 13. The mechanism by which omega-3 fatty acids work in the cardiovascular system may be attributable to the incorporation of omega-3 fatty acids into the cell membranes of the heart. See id. The attached scientific studies demonstrate that consumption of omega-3 fatty acids, in foods and supplements, may reduce the incidence of coronary heart disease. See Exhibits 1 at 145-150. The current scientific evidence in favor of the claim reveals the presently required disclaimer to be anachronistic and inaccurate. See Expert Report of Dr. William Connor (Attached as Exhibit 2). It thus misleads the public and constitutes an unreasonable burden on protected speech. See Zauderer v. Office of Disciplinary Counsel of Supreme Court, 471 U.S. 626, 651 (1985) ("We recognize that unjustified or unduly burdensome disclosure requirements might offend the First Amendment by chilling protected commercial speech."). The current disclaimer states that the scientific evidence in support of the claim is not conclusive. As explained below, it is now generally accepted in the scientific community that omega-3 fatty acids do reduce the risk of coronary heart disease and the science on the point has established the risk reducing effected beyond reasonable doubt. Accordingly, the claim should now be approved by FDA under the significant scientific agreement standard or, if not so approved, at a minimum allowed consistent with the First Amendment but without requiring the present disclaimer.

³ The revised claim and disclaimer read: "Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease. FDA evaluated the data and determined that, although there is scientific evidence supporting the claim, the evidence is not conclusive."

The amended health claim responds to a major public health concern in the United States: coronary heart disease⁴, which is a type of cardiovascular disease.⁵ 21 C.F.R. § 101.75. Coronary heart disease is the leading cause of death in the United States, with 710,760 deaths in 2000. See “National Center for Health Statistics, FASTATS 2000 on Heart Disease,” Center for Disease Control, <http://www.cdc.gov/nchs/fastats/heart.htm> (last visited June 5, 2003) (Attached as Exhibit 3). In the U.S., one of every 5 deaths was from coronary heart disease in 2000. See “Heart Disease and Stroke Statistics—2003 Update,” American Heart Association at 12 (Attached as Exhibit 4). Hence, there were 2,400,000 American deaths in the year 2000, with 1,415,000 of those deaths attributed to cardiovascular disease. See id. Of those cardiovascular disease-related deaths, 54% were attributed to coronary heart disease. See id. at 8. According to the American Heart Association, nearly 2,600 Americans die of cardiovascular disease each day, or one death every thirty-three seconds. See id.

This petition furthers national and HHS policies by identifying a low cost means to help reduce the risk of coronary heart disease. In addition, the petition furthers the recently announced directive of the Office of Management and Budget (“OMB”) to HHS and USDA concerning the health benefits of omega-3 fatty acids. In OMB’s “prompt” letter of May 27, 2003 (Attached as Exhibit 5, wherein Dr. John D. Graham, Administrator, Office of Information and Regulatory Affairs, OMB, writes: “Both epidemiologic and clinical studies find that an increase in consumption of omega-3 fatty acids results in reduced deaths due to CHD”). Dr. John D. Graham further states: “The government should make this life-saving information as widely available as possible.” Id. The truthful, succinct, and accurate health information conveyed by the Petitioners’ amended health claim will enable consumers to make prudent and

⁴ Coronary heart disease includes: heart attack, angina pectoris or both. See Exhibit 5 at 11.

effective dietary choices, cognizant of omega-3 fatty acids' coronary heart disease risk reducing effects. Labeling conventional foods and dietary supplements with the amended omega-3 fatty acids claim will inform consumers at the point of sale of the strong scientific evidence now extant concerning dietary means by which omega-3 fatty acids lessen the risk of coronary heart disease.⁶

Attached hereto and constituting a part of this petition are the following:

A. Preliminary Requirements

1. Omega-3 Fatty Acids meet the definition of 21 C.F.R. § 101.14(b)

The proposed health claims meet the relevant eligibility requirements of 21 C.F.R. § 101.14(b). Section 101.14(b) requires:

(b) Eligibility. For a substance to be eligible for a health claim:

- (1) the substance must be associated with a disease or health-related condition for which the general U.S. population, or an identified U.S. population subgroup (e.g., the elderly), is at risk, or, alternatively, the petition submitted by the proponent of the claim otherwise explains the prevalence of the disease or health-related condition in the U.S. population and the relevance of the claim in the context of the total daily diet and satisfies the other requirements of this section.
- (2) If the substance is to be consumed as a component of a conventional food at decreased dietary levels, the substance must be a nutrient listed in 21 U.S.C. 343(q)(1)(C) or (q)(1)(D), or one that the Food and Drug Administration (FDA) has required to be included in the label or labeling under 21 U.S.C. 343(q)(2)(A); or
- (3) If the substance is to be consumed at other than decreased dietary levels:
 - (i) The substance must, regardless of whether the food is a conventional food or a dietary supplement, contribute taste, aroma, or nutritive value, or any other technical effect listed in § 170.3(o) of this chapter, to the food and must retain that attribute when consumed at levels that are necessary to justify a claim; and
 - (ii) The substance must be a food or a food ingredient or a component of a food ingredient whose use at the levels necessary to justify a claim has been demonstrated by the proponent of the claim, to FDA's satisfaction, to be safe

⁵ Cardiovascular disease includes: coronary heart disease, stroke, congestive heart failure, high blood pressure and congenital cardiovascular defects. See Exhibit 5 at 6.

⁶ The Petitioners view the evidence supportive of omega-3 fatty acids' role in coronary heart disease risk reduction to equal in strength and validity that body of evidence FDA ultimately found supportive of a folic acid/neural tube defect risk reduction claim.

and lawful under the applicable food safety provisions of the Federal Food, Drug and Cosmetic Act.

a. **Omega-3 Fatty Acids are associated with a disease affecting the general U.S. population**

A “disease or health-related condition” means “damage to an organ, part, structure, or system of the body such that it does not function properly (e.g. cardiovascular disease), or a state of health leading to such dysfunctioning (e.g. hypertension); except that diseases resulting from essential nutrient deficiencies (e.g., scurvy, pellagra) are not included in this definition (claims pertaining to such diseases are thereby not subject to § 101.13 or § 101.70).” 21 C.F.R. § 101.14(a)(5). The amended health claim associates the substance, omega-3 fatty acids, with reduction in the risk of coronary heart disease and states its anti-arrhythmic activity.

Coronary heart disease is a cardiovascular disease characterized by narrowing of the coronary arteries, which prevents adequate amounts of blood and oxygen from reaching the heart.⁷ See “Coronary Heart Disease Explained,” National Institutes of Health.

<http://nhlbisupport.com/chd1/chdexp.htm> (last visited June 9, 2003) (Attached as Exhibit 7).

When the heart is deprived of oxygen-carrying blood, angina or heart attack can result. See *id.*

Coronary heart disease is caused by both controllable factors (high blood pressure, high cholesterol, smoking, obesity, physical inactivity, and diabetes) and uncontrollable factors (gender, heredity, and age). See “Facts about Coronary Heart Disease,” National Institutes of Health, <http://www.nhlbi.nih.gov/health/public/heart/other/chdfacts.htm> (last visited June 9, 2003) (Attached as Exhibit 8). Causal factors may act together or in sequence to initiate or promote the onset of coronary heart disease. See *id.*

Cardiovascular disease is the leading cause of death in the United States. See Exhibits 3, 5, 6 and 7. Cardiovascular disease has been the number one killer in the United States every year

since 1900, with the exception of one year: 1918. See Exhibit 4 at 5. In the U.S., one of every 2.5 deaths is from cardiovascular disease. See id. at 8. In 1997, fifteen million new cases of heart disease were diagnosed. See Exhibit 3. In 2000, about 764,100 deaths were attributed to coronary heart disease, more than 2,093 deaths per day. See Exhibit 4 at 5.

The National Heart, Blood, and Lung Institute estimates that the direct and indirect costs of cardiovascular disease in the year 2003 will be \$351.8 billion. See Exhibit 4 at 5. The American Heart Association reports that in 1999, \$26.3 billion in payments were made to Medicare beneficiaries for hospital expenditures related to cardiovascular problems. See id. at 7, *citing* Personal communication with the Centers for Medicare and Medicaid Services, 2002. In 1998, Medicare beneficiaries were paid \$10.6 billion for coronary heart disease alone (\$10,428 per discharge for acute myocardial infarction; \$11,399 per discharge for coronary atherosclerosis; and \$3,617 per discharge for other coronary heart disease claims). See id. at 12, *citing* "Health Care Financing Review, Statistical Supplement [2000]," Centers for Medicare and Medicaid Services. Consequently, reduction in coronary heart disease risk is a health and economic policy necessity for the United States.

b. Omega-3 fatty acids contribute nutritive value at the levels present in supplements and foods

In accordance with section 101.14(b)(3)(i), omega-3 fatty acids contribute nutritive value. While there is no Reference Daily Intake (DRI) for omega-3 fatty acids, the nutritive contribution of omega-3 fatty acids is widely recognized. See Exhibits. 1-2 and 6. The PDR for Nutritional Supplements includes anti-arrhythmic and triglyceride-lowering activities among omega-3 fatty acids' actions and states that omega-3 fatty acids may also have anti-

⁷ This process is known as atherosclerosis.

inflammatory, anti-thrombotic, and immunomodulatory activities. See Exhibit 1 at 145; Exhibit 2 at 13.

Omega-3 fatty acids are naturally occurring lipids found in fish and other marine life. See Exhibit 1 at 145. Although the amount of EPA/DHA in foods and in dietary supplements varies, omega-3 fatty acids from supplements have been reported to be as bioavailable in humans as foods containing omega-3 fatty acids. See Exhibit 1 at 147. The amended health claim does not identify specific intake quantities for omega-3 fatty acids. Studies have measured omega-3 fatty acids supplementation to have nutritive value from 200 mg to 28 grams a day. See Exhibits 2 and 6. Omega-3 fatty acids are typically supplied in solid oral dosage form in capsules containing 400 mg, 500 mg, 1000 mg, 1200 mg, or 2000 mg. See Exhibit 1 at 149. As mentioned above, the omega-3 fatty acids content of food depends upon the type of fish or marine life with per serving amounts varying from 0.2 grams to 3.3 grams. See Exhibit 6 at 12.

c. Omega-3 Fatty Acids are safe and lawful under the FDCA

“For each such ingredient listed, the petitioner should state how the ingredient complies with the requirements of § 101.14(b)(3)(ii), e.g., that its use is generally recognized as safe (GRAS), listed as a food additive, or authorized by a prior sanction issued by the agency, and what the basis is for the GRAS claim, the food additive status, or prior sanctioned status.” 21 C.F.R. § 101.70(f)(A). In accordance with section 101.13(b)(3)(ii), omega-3 fatty acids are both a food and food ingredient and are safe and lawful at the levels necessary to reduce the risk of coronary heart disease. As mentioned above, omega-3 fatty acids are an ingredient of common foods such as cold water fish and other marine life (i.e., plankton). The FDCA deems dietary supplements a food under 21 U.S.C. § 321(ff). Accordingly, omega-3 fatty acids are both a food and a food ingredient under 21 C.F.R. § 101.14(b)(3)(ii).

Omega-3 fatty acids are generally recognized as safe and lawful at the levels necessary to reduce the risk of coronary heart disease. General recognition of safety is based on the views of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food. See 21 C.F.R. § 170.30(a). The basis for such views may be either (1) scientific procedure or (2) in the case of a substance used in food prior to January 1, 1958, through experience based on common use in food. Id.

Safe or safety means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. Safety may be determined by scientific procedures or by general recognition of safety. In determining safety, the following factors shall be considered:

- (1) the probable consumption of the substance and of any substance formed in or on food because of its use.
- (2) The cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in such diet.
- (3) Safety factors which, in the opinion of experts qualified by scientific training and experience to evaluate the safety of food and food ingredients, are generally recognized as appropriate.

21 C.F.R. § 170.3(i).

Omega-3 fatty acids have been a naturally occurring ingredient in foods consumed safely in the United States prior to January 1, 1958. There is no evidence that omega-3 fatty acids consumed either in foods or as dietary supplements have a cumulative effect in the diet that is unsafe. See Exhibit 1 at 149. Interactions may occur between omega-3 fatty acid supplements and aspirin and other non-steroidal anti-inflammatory drugs and herbs (i.e., garlic and ginkgo biloba). See Exhibit 1 at 149. The PDR for Nutritional Supplements states that the most frequently reported adverse reactions associated with consumption of omega-3 fatty acids are increased susceptibility to bruising, nosebleeds, hemoptysis, hematemesis, hematuria and blood in the stool. See id. Nonetheless, the PDR states that most people who consume omega-3 fatty

acids and the above-named drugs and herbs do not suffer from serious adverse reactions. See id.⁸ The PDR indicates no contraindications associated with consumption of omega-3 fatty acids. Id.

The maximum (safe) daily intake of omega-3 fatty acids is generally well above the amount reasonably required to accomplish the intended nutritive effect. 21 C.F.R. § 172.5. The PDR recommends a safe upper limit for omega-3 fatty acids of 5 grams a day for those who have had successful angioplasty and are trying to prevent restenosis; however, a more conservative upper limit of 3 grams a day is recommended for hypertensives who have not been previously treated. See Exhibit 1 at 149. Nutritive effect in reducing the risk of coronary heart disease has been recorded in daily doses ranging from 1 to 28 grams per day, with most studies supplementing at 6 grams per day. See id.; see also Exhibits 2 and 6. Therefore, the amended health claim complies with the safety and lawfulness requirements of 21 C.F.R. § 101.14(b)(3)(ii).

In summary, since omega-3 fatty acids meet the requirements set forth in 21 C.F.R. § 101.14(b), the preliminary requirements of 21 C.F.R. § 101.70 are fully satisfied.

⁸ In this regard, the Petitioners would be willing to include a warning on product labels and labeling that consumers taking non-steroidal anti-inflammatory drugs, such as aspirin, should consult a physician before taking this product.

B. Summary of Scientific Data Supporting the Amended Claim

1. Significant scientific agreement exists to support the amended claim

There is significant scientific agreement among experts who study the effect of omega-3 fatty acids on coronary heart disease that omega-3 fatty acids are an effective modifier (reducer) of the risk of coronary heart disease. See Exhibit 2 at 1; Exhibit 6 at 11. The scientific literature shows that omega-3 fatty acids have triglyceride lowering, anti-arrhythmic, anti-inflammatory and anti-thrombotic effects. See Exhibit 1 at 145; Exhibit 2 at 13; Exhibit 6 at 11.

Although the mechanism of omega-3 fatty acids' anti-arrhythmic activity is not known definitively, omega-3 fatty acids have been shown definitively to produce beneficial physiological and biochemical effects, such as: triglyceride lowering, raising heart rate variability, and reducing fatal arrhythmias. See Exhibit 1 at 146; and Exhibit 6 at 10-11. Omega-3 fatty acids (1) decrease adversely high levels of triglycerides and very low density lipoproteins (thus decreasing the risk of coronary heart disease), (2) increase heart rate variability and thereby decrease the risk of sudden death from heart attack, and (3) help prevent second heart attack in individuals who have sustained a first heart attack. See id. Human clinical trials and epidemiological studies are discussed in the following section.

2. Scientific evidence demonstrates the public health benefits of Omega-3 fatty acids

Since 1999, when FDA requested comments on the relationship between omega-3 fatty acids and coronary heart disease, several major studies have been published that support the claim and render the present required disclaimer unnecessary and inaccurate. Since 2000, eight human clinical trials have evaluated the effects of omega-3 fatty acids consumption on the incidence of coronary heart disease. The most supportive studies are the Harvard Physicians' Study and the Nurses' Health Study. See Exhibit 2 at 2. Last year those studies revealed

baseline blood levels of long-chain n-3 fatty acids to be inversely related to the risk of sudden death. See id. Hence, there was a reduced risk of sudden death in men who had higher blood levels of n-3 fatty acids (EPA and DHA). Similar results were found in the Nurses' Health Study. In the latter, higher intakes of omega-3 fatty acids lowered the risk of coronary heart disease, especially for coronary heart disease deaths. See id. at 3.

The next important clinical trial was the GISSI-PREVENZIONE trial, which was a large clinical trial conducted on patients who had experienced a myocardial infarction. See id. at 4. The study was originally conducted in 1999; however, it was reanalyzed in 2002. In that report, Marchioli, et al. concluded that "the risk of sudden death was significantly prevented by only three months of treatment with fish oil and there was a 67% reduction in overall deaths." Id. Hence, the benefits obtained from consumption of fish oil were profound.

Earlier this year, the Cardiovascular Health Study of Seattle, Washington, published its findings. That population-based prospective cohort study followed 3,910 adults over the course of 9.5 years. See id. at 5. Mozaffarian, et al. found that "there was a 49% lower risk of ischemic heart disease deaths and a 48% lower risk of arrhythmic deaths among persons consuming tuna/other fish three or more times per week compared to those consuming less than once per month." Id. Thus, increased fish consumption directly corresponds to decreased incidence of coronary heart disease.

A review published in 2003 on behalf of the Nutrition Committee of the American Heart Association made the following recommendations: (1) patients without coronary heart disease should consume a variety of preferably oily fish at least twice per week and include foods rich in alpha linolenic acid as well; (2) patients with documented coronary heart disease should consume 1 gm of EPA plus DHA per day, preferably from oily fish or supplements in

consultation with a physician; and (3) patients who need plasma triglyceride lowering should consume 2-4 gm of EPA plus DHA per day, provided as fish oil capsules under a physician's care. See id. at 6.

In addition, eight recent animal studies corroborate the findings of the clinical trials. Id. at 11. Those animal studies have shown the anti-arrhythmic effects of omega-3 fatty acids and conclude that "fish oil fatty acids are a powerful but simple modality to prevent the 300,000 episodes of sudden death occurring in the United States annually." Id. at 12. The most important animal study conclusively found that consumption of n-3 PUFA improved ventricular function by reducing the oxygen required to produce a given work output. See id. at 8

3. Scientific Summary Issues

- a. Is there an optimum level of omega-3 fatty acids to be consumed beyond which no benefit would be expected?

Clinical trials have tested omega-3 fatty acids' effectiveness with doses up to 28 grams per day. See e.g., Exhibit 6 at 11. There is no evidence of an optimum level of omega-3 fatty acids to be consumed beyond which no benefit is expected.

- b. Is there any level at which an adverse effect from the substance or from foods containing the substance occurs for any segment of the population?

There are no serious adverse events reported in conjunction with consumption of omega-3 fatty acids supplements, even up to 15 grams per day of omega-3 fatty acids for prolonged periods of time. See Exhibit 1 at 149. Mild side effects, such as: nausea, diarrhea, halitosis, eructation and "fishy" smelling breath, skin and urine have been reported. See id.⁹

⁹ The Petitioners would accept a warning statement that consumers who experience any adverse effect, including nausea or diarrhea, should discontinue use of this product.

c. Are there certain populations that must receive special consideration?

The PDR for Nutritional Supplements cautions that children, diabetics, pregnant women and nursing mothers should consult a physician before taking omega-3 fatty acids supplements.

See Exhibit 1 at 148.

d. What other nutritional or health factors (both positive and negative) are important to consider when consuming the substance?

Interactions may occur between omega-3 fatty acids supplements and aspirin and other non-steroidal anti-inflammatory drugs and herbs. See id. Those interactions are rare, however, and are eliminated with a lower dose amount of omega-3 fatty acids supplementation. See id.

4. Potential effect of the use of the amended claim on food consumption, including significant alterations in eating habits and corresponding changes in nutrient intakes

The amended claim may increase public intake of omega-3 fatty acids in foods and supplements, including by populations at greater risk of coronary heart disease. The Petitioners do not believe that the amended claim will have any deleterious effect on food consumption or eating habits. The only change in nutrient intake resulting from the amended claim would be for those who choose to supplement their diets with omega-3 fatty acids. The effect on such people is expected to be beneficial, reducing the risk of coronary heart disease, including sudden death heart attacks and saving lives, potentially as many as three hundred thousand per year. See Exhibit 2 at 2.

5. Prevalence of the disease or health-related condition in the U.S. population and the relevance of the claim in the context of the total daily diet.

As discussed above, the amended health claim responds to a major public health concern in the United States: the incidence of, and mortality caused by, coronary heart disease. 21 C.F.R. § 101.75(b). Cardiovascular disease is the leading cause of death in the United States.

See Exhibits 3, 5, 9 and 10. In the U.S., one of every 2.5 deaths is from cardiovascular disease. In 2000, about 764,100 deaths were attributed to coronary heart disease, more than 2,093 deaths per day. See Exhibit 5 at 5. Most studies have shown omega-3 fatty acids supplementation to be effective in coronary heart disease risk reduction at levels of 1-5 grams per day, depending on the patient's condition. See Exhibit 1 at 149; see also Exhibits 2 and 6. Thus, omega-3 fatty acids offer a safe, inexpensive, readily accessible means for reducing the risk of coronary heart disease population wide.

6. Omega-3 Fatty Acids meet the definition of 21 C.F.R. § 101.14(a)

The Petitioners seek FDA approval of the amended claim for use on dietary supplements and foods containing omega-3 fatty acids. Omega-3 fatty acids in foods and dietary supplements meet the definition of a "substance" provided by 21 C.F.R. § 101.14(a): "Substance means a specific food or component of food, regardless of whether the food is in conventional food form or a dietary supplement that includes vitamins, minerals, herbs, or other similar nutritional substances." Omega-3 fatty acids are a group of polyunsaturated fatty acids ("LCPUFA") comprised of eicosapentaenoic acid ("EPA"), docosahexaenoic acid ("DHA"), and linolenic acid ("LNA"). See Exhibit 1 at 145. Omega-3 fatty acids are found in fish and other marine life. See id. These fish oils are rich sources of long-chain polyunsaturated fatty acids of the n-3 (omega-3) type. See Exhibit 1 at 145. The amount of omega-3 fatty acids in foods depends on the source, ranging from 0.2 grams (in flounder) to 3.3 grams (in sardines). See Expert report of Dr. Mary Enig, submitted to FDA on November 22, 1999 with Whitaker, et al. Comments at 12 reincorporated here by reference (Attached as Exhibit 6). Of the numerous fish oils present in cold water fish and other marine life, the two most studied are: eicosapentaenoic acid (EPA; C20:5n-3) and docosahexaenoic acid (DHA; C22:6n-3). See Exhibit 1 at 145. EPA contains

five double bonds, while DHA contains six double bonds. All double bonds are in the *cis* configuration. See id. EPA and DHA are found naturally in the form of triacylglycerols or TAGs. Id. The DHA in the TAGs of fish oil occurs primarily in the sn-2 position (i.e., the middle carbon) of glycerol, while the distribution of EPA is more randomly distributed over all three positions of glycerol. See id.

Omega-3 fatty acids are found in most cold-water fish (i.e., tuna, salmon and mackerel), fish oils (i.e., unhydrogenated menhaden oil), and fish liver oils (i.e., cod liver oil). See Exhibit 6. Omega-3 fatty acids in dietary supplements are most commonly available from fish liver oil (i.e., cod and shark), herring oil, menhaden oil, salmon oil, and tuna oil. See id. at 13. The amounts of EPA and DHA vary depending on the fish source. See id. A more concentrated type of fish oil is also available in the form of a semi-synthetic ethyl ester products that contain 85% EPA/DHA. For example, a one gram ethyl ester capsule contains 490 mg of EPA ethyl ester and 350 mg of DHA ethyl ester. See Exhibit 1 at 149.

Thus, omega-3 fatty acids found in foods and dietary supplements are a "substance" as defined by 21 C.F.R. § 101.14(a).

C. Analytical Method

The amount of omega-3 fatty acids contained in a food or dietary supplement that may be a candidate for bearing the revised health claim can be ascertained by several gas chromatography methods, including: the Association of Official Analytical Chemists' (AOAC) Official Method #991.39: "Fatty Acids in Encapsulated Fish Oils and Fish Oil Methyl and Ethyl Esters." See Exhibit 9. The assay method described in Exhibit 9 is applicable to finished products.

D. Proposed Amended Health Claim

Petitioners propose that the approved model claim for omega-3 fatty acids be amended by removing the disclaimer and permitting its use on foods and dietary supplements containing omega-3 fatty acids. The claim would read as follows:

Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease.

Multiple studies have shown that consumption of omega-3 fatty acid-containing foods and dietary supplements reduce the risk of coronary heart disease. Moreover, recent clinical trials have proven to a near conclusive degree its safety and efficacy for use by the general population.

E. Attachments

Attached are copies of the scientific studies (Exhibit 10) and other information referenced in, and constituting the basis for, this Petition. To the best of the Petitioners' knowledge, all non-clinical studies relied upon were conducted in compliance with the good laboratory practices regulations set forth in 21 C.F.R. Part 58, and all clinical or other human investigations relied upon were either conducted in accordance with the requirements for institutional review set forth at 21 C.F.R. Part 56 or were not subject to such requirements in accordance with 21 C.F.R. § 56.104 or 56.105, and were conducted in conformance with the requirements for informed consent set forth in 21 C.F.R. § 50 et seq. See generally, 21 C.F.R. § 101.7 (c)-(d).

F. Environmental Impact

The requested health claim approval contained in this petition is categorically excluded from the environmental impact statement under 21 C.F.R. § 25.24.

G. Conclusion and Certification

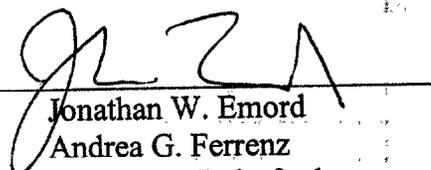
For the foregoing reasons, the Petitioners request that the FDA approve the amended health claim.

Any questions concerning this Petition may be directed to Jonathan W. Emord, Esq. Emord & Associates, P.C., 5282 Lyngate Court, Burke, VA 22015, (202) 466-6937.

The undersigned certify on behalf of the Petitioners that, to the best of their knowledge and belief, the Petition includes all information and views on which the Petitioners rely and is a representative and balanced submission that includes unfavorable information as well as favorable information known by the Petitioners to be pertinent to evaluation of the proposed health claims.

Sincerely,

WELLNESS LIFESTYLES, INC., AND
LIFE EXTENSION FOUNDATION
BUYERS CLUB, INC.

By: 

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Andrea G. Ferrenz
Kathryn E. Balmford
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