

Ray A. Matulka, Ph.D.
Director Toxicology
Burdock Group Consultants
859 Outer Road
Orlando, Florida 32814

RE: Petition for authorized health claim for oleic acid in edible oils and a reduction in the risk of coronary heart disease - Docket Number FDA-2017-Q-0807

Dear Dr. Matulka,

This letter responds to the health claim petition received on November 4, 2016 by the Food and Drug Administration (FDA or we, or the agency), submitted on behalf of Corbion Biotech, Inc. (formerly Terra Via Holdings, Inc.) pursuant to Sections 403(r)(4) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §§ 343(r)(4)). The petition requested that the agency authorize a health claim characterizing the relationship between the consumption of oleic acid in edible oils and reduced risk of coronary heart disease (CHD).

The petition proposed the following language for the claim:

“Daily consumption of edible oil with at least 10 grams of oleic acid *per* serving (one tablespoon) reduces the risk of coronary heart disease. To achieve this benefit, oleic acid containing oils with at least 10 grams of oleic acid *per* serving should replace a similar amount of saturated fat and not increase the total number of calories you eat in a day. One serving of [x] oil provides [x] grams of oleic acid (which is [x] grams of monounsaturated fatty acid).”

FDA evaluated the scientific evidence provided with the petition and other evidence related to your proposed claim. Based on this review, FDA determined that the scientific evidence supporting the proposed health claim did not meet the “significant scientific agreement” standard under § 403(r)(3)(B)(i) of the Act for conventional foods (21 CFR 101.14(c)). FDA notified you of this decision on February 10, 2017, and in a letter dated February 13, 2017, the petitioner agreed to having the petition reviewed as a qualified health claim petition. FDA considers this request as the petitioner choosing to seek FDA review of the petition as a qualified health claim petition. Thus, FDA filed the petition on February 21, 2017 as a qualified health claim petition, with the Docket number FDA-2017-Q-0807 and posted it on the Regulations.gov website for a 60-day comment period, consistent with the agency’s guidance for procedures on qualified health claims.¹ The agency received three comments all of which supported the claim requested in the petition.

This letter sets forth the results of FDA’s scientific review of the evidence for the requested qualified health claim, as well as the basis of FDA’s determination that the current evidence

¹ See FDA “Interim Procedures for Qualified Health Claims in the Labeling of Conventional Human Food and Human Dietary Supplements” (July 10, 2003) [<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/LabelingNutrition/ucm053832.htm> (accessed June 6, 2018)].

supports a qualified health claim concerning the relationship between oleic acid in edible oils and a reduced risk of CHD. Accordingly, this letter discusses the factors that FDA intends to consider in the exercise of its enforcement discretion for a qualified health claim with respect to the consumption of oleic acid in edible oils and a reduced risk of CHD.

I. Overview of Data and Eligibility for a Qualified Health Claim

A health claim characterizes the relationship between a substance and a disease or health-related condition (21 CFR 101.14(a)(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, is at risk (21 CFR 101.14(b)(1)). Health claims characterize the relationship between the substance and a reduction in risk of contracting a particular disease or health-related condition.² In a review of a qualified health claim, the agency first identifies the substance and disease or health-related condition that are the subject of the proposed claim and the population to which the claim is targeted.³

FDA considers the data and information provided in the petition, in addition to other written data and information available to the agency, to determine whether the data and information could support a relationship between the substance and the disease or health-related condition.⁴ The agency then separates individual reports of human studies from other types of data and information. FDA focuses its review on reports of human intervention and observational studies.⁵

In addition to individual reports of human studies, the agency also considers other types of data and information in its review, such as meta-analyses⁶, review articles⁷, and animal and *in vitro* studies. These other types of data and information may be useful to assist the agency in understanding the scientific issues about the substance, the disease, or both, but cannot by themselves support a health claim relationship. Reports that discuss a number of different studies, such as meta-analyses and review articles, do not provide sufficient information on the individual studies reviewed for FDA to determine critical elements, such as the study population characteristics and the composition of the products used. Similarly, the lack of detailed information on studies summarized in review articles and meta-analyses prevents FDA from

² See *Whitaker v. Thompson*, 353 F.3d 947, 950-51 (D.C. Cir.) (upholding FDA's interpretation of what constitutes a health claim), cert. denied, 125 S. Ct. 310 (2004).

³ See FDA, "Guidance for Industry: Evidence-Based Review System for the Scientific Evaluation of Health Claims - Final," January 2009 [<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/LabelingNutrition/ucm073332.htm> (accessed May 10, 2017)].

⁴ For brevity, "disease" will be used as shorthand for "disease or health-related condition" in the rest of this letter except when quoting or paraphrasing a regulation that uses the longer term.

⁵ In an intervention study, subjects similar to each other are randomly assigned to either receive the intervention or not to receive the intervention, whereas in an observational study, the subjects (or their medical records) are observed for a certain outcome (i.e., disease). Intervention studies provide the strongest evidence for an effect. See *supra*, note 3.

⁶ A meta-analysis is the process of systematically combining and evaluating the results of clinical trials that have been completed or terminated (Spilker, 1991).

⁷ Review articles summarize the findings of individual studies.

determining whether the studies are flawed in critical elements such as design, conduct of studies, and data analysis. FDA must be able to review the critical elements of a study to determine whether any scientific conclusions can be drawn from it. Therefore, FDA uses meta-analyses, review articles, and similar publications⁸ to identify reports of additional studies that may be useful to the health claim review and as background about the substance-disease relationship.⁹ If additional studies are identified, the agency evaluates them individually.

FDA uses animal and *in vitro* studies as background information regarding mechanisms of action that might be involved in any relationship between the substance and the disease. The physiology of animals is different than that of humans. *In vitro* studies are conducted in an artificial environment and cannot account for a multitude of normal physiological processes, such as digestion, absorption, distribution, and metabolism, which affect how humans respond to the consumption of foods and dietary supplements.¹⁰ Animal and *in vitro* studies can be used to generate hypotheses or to explore a mechanism of action but cannot adequately support a relationship between the substance and the disease.

FDA evaluates the individual reports of human studies to determine whether any scientific conclusions can be drawn from each study. The absence of critical factors, such as a control group or a statistical analysis, means that scientific conclusions cannot be drawn from the study (Spilker, 1991). Studies from which FDA cannot draw any scientific conclusions do not support the health claim relationship, and these are eliminated from further review.

Because health claims involve reducing the risk of a disease in people who do not already have the disease that is the subject of the claim, FDA considers evidence from studies in individuals diagnosed with the disease that is the subject of the health claim only if it is scientifically appropriate to extrapolate to individuals who do not have the disease. That is, the available scientific evidence must demonstrate that: (1) the mechanism(s) for the mitigation or treatment effects measured in the diseased populations are the same as the mechanism(s) for risk reduction effects in non-diseased populations; and (2) the substance affects these mechanisms in the same way in both diseased people and healthy people. If such evidence is not available, the agency cannot draw any scientific conclusions from studies that use diseased subjects to evaluate the substance-disease relationship.

Next, FDA rates the remaining human intervention and observational studies for methodological quality. This quality rating is based on several criteria related to study design (e.g., use of a placebo control versus a non-placebo controlled group), data collection (e.g., type of dietary assessment method), the quality of the statistical analysis, the type of outcome measured (e.g., disease incidence versus validated surrogate endpoint), and study population characteristics other than relevance to the U.S. population (e.g., selection bias and whether important information about the study subjects – e.g., age, smoker vs. non-smoker – was gathered and reported). For example, if the scientific study adequately addressed all or most of the above criteria, it would receive a high methodological quality rating. Moderate or low quality ratings would be given

⁸ Other examples include book chapters, abstracts, letters to the editor, and committee reports.

⁹ Certain meta-analyses may be used as part of the health claim review process. See *supra*, note 3.

¹⁰ Institute of Medicine (2005). Dietary Supplements: A Framework for Evaluating Safety. Chapter 7, Categories of Scientific Evidence – In Vitro Data.

based on the extent of the deficiencies or uncertainties in the quality criteria. Studies from which FDA cannot draw scientific conclusions cannot be used to support the health claim relationship, and therefore are eliminated from further review. Finally, FDA evaluates the results of the remaining studies. The agency then rates the strength of the total body of publicly available evidence.¹¹ The agency conducts this rating evaluation by considering the study type (e.g., intervention, prospective cohort, case-control, cross-sectional), the methodological quality rating previously assigned, the quantity of evidence (number of studies of each type and study sample sizes), whether the body of scientific evidence supports a health claim relationship for the U.S. population or target subgroup, whether study results supporting the proposed claim have been replicated,¹² and the overall consistency¹³ of the total body of evidence.¹⁴ Based on the totality of the scientific evidence, FDA determines whether such evidence is credible to support a qualified health claim for the substance-disease relationship, and, if so, considers what qualifying language should be included to convey the limits on the level of scientific evidence supporting the relationship or to prevent the claim from being misleading in other ways.

A. Substance

A health claim characterizes the relationship between a substance and a disease or health-related condition (21 CFR 101.14(a)(1)). A substance means a specific food or component of a food, regardless of whether the food is in conventional form or a dietary supplement that includes vitamins, mineral, herbs, or other similar nutritional substances (21 CFR 101.14(a)(2)). The petition identified oleic acid in edible oils containing at least 70% of oleic acid per serving¹⁵ (throughout this letter we may refer to these oils with at least 70% of oleic acid per serving as “high oleic acid oils”) as the substance that is the subject of the proposed claim. Oleic acid is a monounsaturated fatty acid (MUFA) and is a component of edible oils traditionally consumed in the United States. Oleic acid can be found naturally in numerous food sources, including edible oils, meat (e.g., beef, chicken, and pork), cheese, nuts, seeds (e.g., sunflower), eggs, pasta, milk, olives, and avocados (USDA, 2018). The petition identified the following edible oils that contain at least 70% of oleic acid per serving: 1) high oleic sunflower oil, 2) high oleic safflower oil, 3) high oleic canola oil, 4) olive oil, and 5) high oleic algal oil.

Therefore, the agency concludes that oleic acid in edible oils containing at least 70% of oleic acid per serving is a component of food and thus meets the definition of a substance in the health claim regulation (21 CFR 101.14(a)(2)).

B. Disease or Health-Related Condition

¹¹ See *supra*, note 3.

¹² Replication of scientific findings is important for evaluating the strength of scientific evidence (Wilson, 1990).

¹³ Consistency of findings among similar and different study designs is important for evaluating causation and the strength of scientific evidence (Hill AB. 1965); see also Agency for Healthcare Research and Quality, “Systems to rate the scientific evidence” (March 2002) [<http://archive.ahrq.gov/clinic/epcsums/strengthsum.pdf> (accessed May 10, 2017)], defining “consistency” as “the extent to which similar findings are reported using similar and different study designs.”

¹⁴ See *supra*, note 3.

¹⁵ It also can be referred as an edible oil with at least 10 grams of oleic acid per serving (tablespoon).

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 or a state of health leading to such dysfunctioning (21 CFR 101.14(a)(5)). The petition has identified coronary heart disease (CHD) as the disease or health-related condition that is the subject of the proposed claim. The agency concludes that coronary heart disease is a disease and therefore the petitioner has satisfied the requirement in 21 CFR 101.14(a)(5).

C. Safety Review

Under 21 CFR 101.14(b)(3), if the substance is to be consumed at other than decreased dietary levels, 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 21 CFR 170.3(o) to the food and must retain that attribute when consumed at levels that are necessary to justify a claim (21 CFR 101.14(b)(3)(i)). 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 the claim must be demonstrated by the proponent of the claim, to FDA's satisfaction, to be safe and lawful under the applicable food safety provisions of the Federal Food, Drug, and Cosmetic Act (the Act). For conventional foods, this evaluation involves considering whether the ingredient that is the source of the substance is generally recognized as safe (GRAS), approved as a food additive, or authorized by a prior sanction issued by FDA (see 101.70(f)).

The petitioner asserts that oleic acid is a component of food ingredients that provides nutritive value in the diet. The definition of "nutritive value" means "a value sustaining human existence by such processes as promoting growth, replacing loss of essential nutrients, or providing energy." (21 CFR 101.14(a)(3)). Edible oils containing oleic acid provide nutritive value to the diet by serving as a source of energy. Like all dietary fats, edible oils containing oleic acid provide 9 kcal/g of energy. FDA agrees that oleic acid in edible oils contributes nutritive value.

In order to receive a possible benefit from consumption of high oleic acid-containing oils and reduced risk of CHD, the scientific evidence suggests that the daily minimum amount of oleic acid that should be consumed in place of fats and oils higher in saturated fatty acids (SFA), while not increasing caloric intake is about 15 g of oleic acid, which corresponds to about 20 g of oleic acid-containing oils that contain at least 70% oleic acid per serving. Twenty grams of high oleic acid-containing edible oils (containing at least 70% of oleic acid per serving) is about 1½ tablespoons. Because the qualified health claim, in accordance with the petition and the scientific evidence, specifies that high oleic acid-containing edible oil is to replace SFA in the diet while not increasing caloric intake, an individual's SFA intake should not increase based on the recommendations in the claim (see Section V.).

The petitioner also asserted that oleic acid, as a component of other foods, has a long history of consumption in the United States and around the world. The Select Committee on GRAS Substances (SCOGS) report Number 65 indicates that oleic acid has been used as foods or as components of food, such as olive oil, by man for many years (SCOGS, 1977). Oleic acid is the most common MUFA and approximately 92 percent of MUFA are oleic acid¹⁶ (IOM, 2002a).

¹⁶ In most of the articles, reviewed for this health claim, approximately 98 percent of MUFA were oleic acid.

The Institute of Medicine (IOM) has not set an Adequate Intake, an Estimated Average Requirement, or a Recommended Dietary Allowance for MUFA because there is no evidence to indicate that MUFA are essential in the diet, and MUFA are synthesized by the body and have no known independent role in preventing chronic diseases (IOM, 2002a). Based on the lack of data on adverse effects of MUFA, a Tolerable Upper Intake Level has not been set (IOM, 2002a). The IOM has, however, set an Acceptable Macronutrient Distribution Range (AMDR) for total fat, which is 20 to 35% of total energy (IOM, 2002a). Based on data in the Continuing Survey of Food Intakes by Individuals, 1994-1996, 1998, the median MUFA intake ranged from approximately 25 to 39 g per day for men and 18 to 24 g per day for women. The mean daily intake of MUFA in the United States for all individuals, excluding pregnant and/or lactating women is 28.7 g, which corresponds to 258 calories (IOM, 2002b). Data from the 1987 - 1988 Nationwide Food Consumption Survey indicated that mean intakes of MUFA were 13.6 to 14.3% of energy (IOM, 2002a).

Oleic acid can be found in a variety of foods that are commonly consumed, including meats, vegetables, fruits, and vegetable oils. As a source of oleic acid, olive oil use dates back to the Bronze Age (approximately 3,500 to 1,200 B.C) where cultivation of the olive in the Mediterranean region flourished (Kiple and Ornelas, 2000). Olive cultivation in California began producing olives for oil production at the beginning of the 20th century (Kiple and Ornelas, 2000). Sunflowers, while originating in the Americas, were transplanted to Europe and were cultivated for oilseed, including in Russia, where high-oleic sunflower oil originated in the mid-1970s (Kiple and Ornelas, 2000). Canola oil (a variety of rapeseed oil) was cultivated in India as far back as 3,000 years ago and, more recently, in Canada and the United States, and select varieties have been cultivated to produce oils with high levels of oleic acid. Oleic acid consumption is not limited to food to which it is added as a cooking oil. Foods such as avocados, milk, cheese, and meat also contain oleic acid in various amounts (USDA, 2018).

Oleic acid has been authorized for direct addition to food under 21 CFR 172.860. Oleic acid may be used safely in foods as a lubricant, binder, and as a defoaming agent in accordance with good manufacturing practice, and as a component in the manufacture of other food-grade additives (21 CFR 172.860).

Oleic acid provides nutritive value, is a ubiquitous, natural component of the food supply, and has been approved as a direct additive to foods; and the level of oleic acid in edible oils containing at least 70% oleic acid per tablespoon necessary to justify the claim should not increase an individual's saturated fat intake due to the replacement of SFA in the diet. Therefore, FDA concludes under the preliminary requirements in 21 CFR 101.14(b)(3)(ii), that oleic acid in edible oils containing at least 70% oleic acid per tablespoon at the levels necessary to justify the claim is safe and lawful.

II. The Agency's Consideration of a Qualified Health Claim

FDA has identified the following disease endpoints to use in identifying CHD risk reduction for purposes of a health claim evaluation: the incidence of coronary events (myocardial infarction (MI), ischemia), cardiovascular death, coronary artery disease, and atherosclerosis. In addition,

the following surrogate endpoints have been identified by FDA for evaluating CHD risk reduction for the purposes of a health claim: change in blood pressure, blood (serum or plasma) concentrations of total cholesterol (TC), and blood (serum or plasma) concentrations of low density lipoprotein cholesterol (LDL-C).¹⁷ These disease and surrogate endpoints were used to evaluate the potential effects of oleic acid on CHD risk.

The petition cited 69 publications in their letter as evidence to substantiate the relationship for the proposed claim (see Docket number FDA-2017-Q-0807). These publications included 14 review articles, one animal study, three reports on classification of fats and oils, or the chemical composition and structure of fats, 23 documents from government agencies or other professional associations, four publications that did not evaluate the disease that was the subject of this petition, one study on supporting the use of a minimum of three weeks study duration for intervention studies that measure cholesterol and LDL-C levels (Kris-Ethernton and Dietschy, 1997), and one study (Kwon et al., 1991) that was used as a reference to determine the percent of oleic acid in olive oil in another study (Wardlaw et al., 1991), and 22 intervention studies that evaluated high oleic acid intake (at least 70% of oleic acid per serving)¹⁸ and risk reduction of CHD. We also assessed all abstracts and publications that were identified by the petition through their systematic review that were excluded in the petition based on their inclusion and exclusion criteria (Appendix I, II, III, IV, VI of the petition, Docket number FDA-2017-Q-0807). We also determined that scientific conclusions could not be drawn, from these publications, about a relationship between the intake of high oleic acid and CHD risk. We identified five additional intervention studies through a literature search that evaluated the relationship between high oleic acid intake and risk of CHD (Binkoski et. al., 2005; Choudhury et al., 1995; Mensink et al., 1987; Ng et al., 1992; Zock et al., 1994). Therefore, we evaluated a total of 27 intervention studies to substantiate a relationship for the proposed claim.

A. Assessment of Review Articles and Other Background Materials

“Background materials” here refers to review articles, and reports from federal agencies and professional associations. Although useful for background information and identifying additional studies, these materials do not contain sufficient information on the individual studies that they reviewed and, therefore, FDA could not draw any scientific conclusions from this information. For example, FDA could not determine factors such as the study population characteristics or nutrient composition of experimental diets. Similarly, the lack of detailed information on studies summarized in these materials prevents FDA from determining whether the studies are flawed in critical elements such as design, conduct of studies, and data analysis. FDA must be able to review the critical elements of a study to determine whether any scientific conclusions can be drawn from it. As a result, the background materials supplied by the petitioner do not provide information from which scientific conclusions can be drawn regarding the substance-disease relationship claimed by the petitioner.

¹⁷ National Heart, Blood and Lung Institute (NHLBI), Heart and Blood Vessel Diseases [http://www.nhlbi.nih.gov/health/dci/Diseases/Atherosclerosis/Atherosclerosis_WhatIs.html] and National Cholesterol Education Program, U.S. Department of Health and Human Services, 2001 [<http://www.nhlbi.nih.gov/files/docs/resources/heart/atp-3-cholesterol-full-report.pdf>]. (Accessed June 6, 2018).

¹⁸ High oleic acid means oils that contain at least 70% oleic acid per serving (i.e., one tablespoon).

B. Assessment of Animal Studies

FDA uses animal studies as background information regarding mechanisms of action that might be involved in any relationship between the substance and the disease, and they can also be used to generate hypotheses or to explore a mechanism of action, but they cannot adequately support a relationship between the substance and the disease in humans. FDA did not consider the animal studies cited with the petition as providing any supportive information about the substance-disease relationship because such studies cannot mimic the normal human physiology that may be involved in the risk reduction of CHD, nor can the studies mimic the human body's response to the consumption of edible oils containing at least 70% of oleic acid. Therefore, FDA could not draw any scientific conclusions regarding high oleic acid intake and the reduction of risk of CHD from the animal study cited in the petition.

C. Assessment of Intervention Studies

FDA evaluated 27 studies that investigated the relationship between consumption of high oleic acid and risk of CHD. Of these 27 studies, scientific conclusions could not be drawn from 20 studies.

Ten studies either did not report the exact amount of oleic acid or did not provide a high oleic acid edible oil (with at least 70% of oleic acid per serving), which is the substance that is the subject of this petition.^{19,20} As discussed above, the substance that is the subject of this petition is oleic acid in high oleic acid edible oil containing at least 70% of oleic acid per serving. For these reasons, scientific conclusions could not be drawn from these ten studies.

Ten studies did not include a control group or used an inappropriate control group to support the proposed claim.²¹ Without an appropriate control group, it cannot be determined whether changes in the endpoints of interest are due to the replacement of SFA with high oleic acid oil or due to unrelated and uncontrolled extraneous factors (Spilker, 1991). In assessing the appropriateness of the control for this qualified health claim, we considered the differences in the fatty acid composition between the high oleic acid-containing vegetable oil and the control diet. The differences in the fatty acid composition should reflect the differences in fatty acids that result from substituting edible oils containing high oleic acid for sources of SFA (e.g., similar or lower amounts of SFA, and higher amounts of oleic acid in the high oleic acid oil diet compared with the control diet). Otherwise, the control diet is inappropriate for evaluating the replacement of SFA with MUFA from high oleic acid-containing oil, and scientific conclusions cannot be drawn from such studies.

¹⁹ Binkoski et al., 2005; Fuentes et al., 2001, 2008; Jansen et al., 2000; Kris-Etherton et al., 1993, 1999; Mensink et al., 1987; Ng et al., 1992; Nydahl et al., 1994; Wardlaw et al., 1991.

²⁰ In this section, significant flaws in the reports of these studies from which scientific conclusions could not be drawn are generally discussed. Such studies may have other flaws in addition to those specifically mentioned.

²¹ Castaner et al., 2012; Castro et al., 2000; Gimeno et al., 2007; Hernaez et al., 2014; Marrugat et al., 2004; Moreno-Luna et al., 2012; Perez-Jimenez et al., 1995; Perona et al., 2011;; Reaven et al., 1993; Silva et al., 2014.

Consequently, scientific conclusions could not be drawn from a total of 20 studies about the relationship between intake of edible oils containing high oleic acid (at least 70% of oleic acid per serving) and risk of CHD. Scientific conclusions could be drawn from seven²² of the 27 publications. The seven publications describe eight analyses of intervention studies that evaluated the relationship between high oleic acid edible oil consumption and risk of CHD.

Gillingham et al. (2011) conducted a moderate quality randomized, crossover, single blind, controlled-feeding study in 36 Canadian hypercholesterolemic men (n=13) and women (n=23), with a mean age of 47.5 ± 11.9 (SD)²³ years old (range 18 to 65 years). Baseline mean value for serum TC and LDL-C was 5.94 mmol/L and 3.70 mmol/L,²⁴ respectively. Participants were fed diets containing either high oleic canola (rapeseed) oil, which contains about 74% oleic acid per serving, SFA: 5.6% of energy intake), a 1:1 blend of the high oleic canola oil and flaxseed oil (approximately 55% alpha linoleic acid, high polyunsaturated fatty acid (PUFA, SFA: 6.1% of energy intake), or a western diet (control, SFA:11.2% of energy intake) as part of an isocaloric controlled diet for 4 weeks each. The high oleic acid diet significantly lowered TC and LDL-C (5.27 ± 0.14 , 3.1 ± 0.12 mmol/L, respectively) compared with the control diet that had higher SFA (5.65 ± 0.16 , 3.53 ± 0.14 mmol/L, respectively) ($P < 0.01$).²⁵ At the end of the 4 weeks intervention, the high oleic acid group had significantly higher level of serum TC compared to the high PUFA group.

Mata et al. (1997) was a moderate quality nonrandomized, non-blinded crossover controlled feeding study in normocholesterolemic premenopausal (n=13) and postmenopausal (n= 8) women from Spain, with a mean age of 43.3 ± 12.5 (SD) years. The TC and LDL-C at baseline in women regardless of menopausal state was 4.94 ± 0.83 mmol/L and 2.92 ± 0.62 mmol/L, respectively. Women first consumed a palm oil diet (control, SFA: ~18% of energy intake) for 4 weeks, and then they consumed either an olive oil diet high in oleic acid (about 79% oleic acid, SFA: ~10% of energy) and sunflower oil (high in PUFA, SFA: ~10% of energy) for 6 weeks each. Diets in each of the three periods were the same with only the type of oils used in the preparation of the meals differing between the groups. All meals were prepared at the community's kitchen and consumed in the dining hall. The high oleic acid oil diet in all women, regardless of menopausal state, significantly decreased TC and LDL-C (mean \pm SD, 4.80 ± 0.85 mmol/L, 2.80 ± 0.62 mmol/L, respectively) compared to the control diet (5.27 ± 0.85 mmol/L, 3.44 ± 0.70 mmol/L, respectively) ($P < 0.001$). However, the statistical analyses were not reported on the effect of high oleic acid consumption on TC and LDL-C compared to control group in each of premenopausal or postmenopausal subgroups. Both TC and LDL-C were significantly higher in postmenopausal women compared to premenopausal women ($P < 0.05$). No significant differences in TC, or LDL-C were observed between high oleic acid and high PUFA groups.

²² Gillingham et al., 2011 Mata et al., 1997; Choudhury et al., 1995; Kien et al., 2014; Lichtenstein et al., 1993; Mattson and Grundy, 1985; Zock et al., 1994.

²³ Standard deviation

²⁴ For conversion of mmol/L to mg/dL multiply by 38.7.

²⁵ For the outcome of a study to demonstrate a statistically significant difference between groups, P must be < 0.05 . See *supra*, note 3.

Choudhury et al. (1995) conducted a moderate quality randomized, crossover study in 21 Australian normocholesterolemic men ($n=11$, mean \pm SD, 27.9 ± 9 years) and women ($n=10$, 27.7 ± 7.8 years). The baseline TC and LDL-C were 5.53 ± 1.11 and 3.63 ± 1.37 , respectively. These subjects consumed diets containing either palmolein oil (control, SFA: ~ 13.3 % of energy intake), or olive oil (about 77 % of oleic acid, SFA: ~ 8 % of energy intake) for each period of study (about 4 weeks). Subjects received individual dietary counseling before the start of the study and were required to replace most of their usual fat intake with either palmolein or olive oil containing high levels of oleic acid. Dietary fats from other sources (e.g., butter, margarine, cooking oils, nuts, cream, eggs, baked goods and skin of poultry) were minimized. Food intakes were monitored by daily food records throughout each period and body weight was recorded regularly. During the study, there were no significant differences in energy, protein, carbohydrates, fat or cholesterol intake between the two diet groups. Furthermore, no significant difference in body weight was observed between the two diet groups. After approximately 4 weeks of consuming the two diets, there were no significant differences in TC and LDL-C between the control (4.65 ± 1.26 mmol/L, 3.33 ± 1.13 mmol/L, respectively) and high oleic acid diet (4.63 ± 0.99 mmol/L, 3.41 ± 0.96 mmol/L, respectively) diets.

The study by Kien et al. (2014) was a moderate quality randomized, crossover, controlled feeding study in 18 white U.S. adults (9 men (mean \pm SD 28.9 ± 2.53 years); 9 women (30 ± 2.2 years)). Participants consumed a low fat and low palmitic acid for 7 days and then participated in a cross over study of 3 weeks diet of high palmitic acid (control diet, SFA: 16% of energy intake) or olive oil high in oleic acid (about 75 % oleic acid, SFA: ~ 2.4 % of energy intake). Except for the test oils, the foods were identical in both diets. The test oils were not used for cooking but were mixed with food that had been warmed. The TC and LDL-C levels were significantly decreased after consuming the high oleic acid diet compared to the control diet ($P < 0.01$).

The study by Lichtenstein et al. (1993) was a moderate quality, randomized, double blind, crossover feeding study of 15 U.S. adults (6 men and 8 postmenopausal women) with a mean age of 61 years old (range 44 to 78 years). The LDL-C level ranged from 133 to 219 mg/dL.²⁶ The purpose was to assess the effects of diets containing oils relatively high in oleic acid or PUFA as part of the National Cholesterol Education Program (NCEP) step 2 diets.²⁷ All subjects initially received a western diet (considered as the control diet, SFA: ~ 13 % of energy intake) for four weeks without any randomization. Subjects then were randomized to receive the three-vegetable oils diets (canola (SFA: ~ 5.4 % of energy intake), corn (SFA: ~ 6.9 % of energy intake) or high oleic acid olive oil (about 71% of oleic acid, SFA: ~ 6.9 % of energy intake)) enriched diets designed to meet the NCEP Step 2 guidelines. All foods and drinks were provided by the metabolic research unit for consumption on site or were packaged for take-out. All experimental diets were identical, except for test oils. The chemical analysis of composition of the study diets showed that the control diet was lower in carbohydrate (48 ± 2.9 % of energy intake), and higher in fat (35.4 ± 2.4 % of energy intake) than the high oleic acid diet (carbohydrate, 52.8 ± 3.9 % of energy intake; fat, 30 ± 2.8 % of energy intake). The control group diet also had higher amounts

²⁶ For conversion from mg/dL to mmol/L divide by 38.7.

²⁷ NCEP Step II diet contains about 55% or more of calories from CHO, 30% or less of calories from fat (with less than 7% from SFA, up to 10% PUFA, up to 15% MUFA) and less than 200 mg/day of cholesterol.

of PUFA (7.94 ± 0.75 % of energy intake) compared to the high oleic acid diet (3.85 ± 0.34 % of energy intake). The TC and LDL-C levels were significantly lower after consumption of the high oleic acid diet (mean \pm SD, 205 ± 19 mg/dL, 132 ± 19 mg/dL, respectively) compared to the control diet (221 ± 32 mg/dL, 152 ± 29 mg/dL, respectively) groups. No significant differences in LDL-C were observed between high oleic acid and either canola or corn oil groups. However, the TC level was statistically reduced in canola oil or corn oil compared to olive oil.

The study by Mattson and Grundy (1985) was a moderate quality, randomized, crossover design study conducted at two U.S medical centers and on 20 patients (47-69 years) with a history of heart disease²⁸ and mean TC level of 263 ± 50 mg/dL. All subjects received a liquid formula diet²⁹ which provided 40% of energy intake as fat, 44% as carbohydrate, and about 16% as protein. The sole fat contents were either from palm oil (control, SFA: 49.7 % of liquid diet),³⁰ high oleic safflower oil (about 73% of oleic acid, SFA: \sim 8.6% of liquid diet), or high-linoleic safflower oil (high PUFA, SFA: \sim 11% of liquid diet). Calorie intake was adjusted as needed to maintain the initial body weight. The serum concentration of TC and LDL-C was significantly reduced in subjects who consumed high oleic acid diet (mean \pm SEM³¹, 197 ± 6 mg/dL, 119 ± 8 mg/dL, respectively) compared to the control (224 ± 10 mg/dL, 143 ± 11 mg/dL, respectively). No significant differences in LDL-C or TC were observed between high oleic acid and high PUFA groups.

Zock et al. (1994) conducted a moderate quality randomized, crossover, single blind, feeding study of 23 men (mean = 28 years (18- 62 years)) and 36 women (mean = 29 years (18 - 55 years)) in the Netherlands. Baseline serum TC levels ranged from 3.67 to 7.10 mmol/L (mean = 5.06 mmol/L). Participants randomly received either diets containing high SFA: palmitic acid (control 1, SFA: 21% of energy intake) or myristic acid (control 2, SFA: 21.3% of energy intake) or high oleic sunflower oil (about 70% of oleic acid, SFA: 10.8% of energy intake) for a period of three weeks each. All foods were provided to participants and were similar except in the assigned test oils. TC and LDL-C levels were significantly reduced with high oleic acid consumption (mean \pm SD, 4.53 ± 0.81 mmol/L, 2.6 ± 0.7 , mmol/L respectively) compared to either the palmitic acid control diet (4.96 ± 0.85 mmol/L, 2.98 ± 0.72 mmol/L, respectively), or the myristic acid control diet (5.19 ± 0.9 mmol/L, 3.09 ± 0.78 mmol/L, respectively) ($P < 0.02$).

D. Assessment of Observational Studies

There were no observational studies that evaluated the relationship between high oleic acid consumption and risk of CHD.

III. Strength of the Scientific Evidence

²⁸ None had recent myocardial infarction, unstable angina pectoris, or congestive heart failure.

²⁹ Composition of 1000 kcal liquid formula diet (gram): fat 43.7, monoglyceride 0.9, skim milk powder 106.6, dextrose 43.7, cellulose 10, water 563, vanilla flower 29 (Mattson et al., 1982).

³⁰ The total calorie and % of calorie for each fatty acid are not reported.

³¹ SEM= standard error of mean

Below, the agency rates the strength of the total body of publicly available evidence. The agency conducts this rating evaluation by considering the study type (e.g., intervention, prospective cohort, case-control, cross-sectional), the methodological quality rating previously assigned, the number of studies and number of subjects per group, whether the body of scientific evidence supports a health claim relationship for the U.S. population or a target subgroup, whether study results supporting the proposed claim have been replicated,³² and the overall consistency³³ of the total body of evidence.³⁴ Based on the totality of the scientific evidence, FDA determines whether such evidence is credible to support a qualified health claim for the substance-disease relationship and, if so, considers what qualifying language should be included to convey the limits on the level of scientific evidence supporting the relationship or to prevent the claim from being misleading in other ways.

As discussed in Section II, the totality of the scientific evidence for a relationship between edible oils containing at least 70% oleic acid per serving and CHD risk includes seven publications describing eight analyses of intervention trials. All seven studies included small samples sizes (range 15 to 59 subjects per study). Furthermore, all studies were of moderate methodological quality. One study (Mattson and Grundy, 1985) used liquid formula diet with various oils. This diet has limited applicability to the healthy U.S. populations, due to the differences in the composition of the typical U.S. diet versus a liquid formula diet, which is not typically consumed by the U.S. population. The studies were conducted in individuals with baseline TC and LDL-C that ranged from normal to high, which were considered healthy normocholesterolemic or hypercholesterolemic subjects. One study was conducted in 20 patients with a history of atherosclerotic disease (Mattson and Grundy, 1985).³⁵ The studies were conducted in the U.S. and Canada as well as a variety of other developed countries. Six studies demonstrated a lowering of TC and LDL-C with the edible oil containing high oleic acid, and one study showed no significant effect of oleic acid on TC and LDL-C levels. One study (Mata et al., 1997) showed that both TC and LDL-C were significantly higher in postmenopausal women than premenopausal women ($P < 0.05$); however, statistical analyses were not conducted between high oleic acid diet and the SFA diet in these subgroups. Most importantly, none of the intervention studies suggested that edible oils containing high oleic acid (MUFA), independent of SFA displacement in fats and oils, would lower TC and LDL-C levels. Therefore, the favorable impact of lowering the TC and LDL-C may be due to the decreased levels of SFA in fats and oils and not an independent effect of consumption of edible oils containing at least 70% of oleic acid per serving.

Based on FDA's review of the strength of the total body of scientific evidence for the proposed qualified claim, FDA concludes that the scientific evidence is credible and supports the substance/disease relationship. However, due to the small number of studies with a moderate methodological quality, the small number of subjects per study, one study providing a liquid formula diet that is not representative of diets consumed by the healthy U.S. population, one study that did not show any effect of high oleic acid edible oil on TC and LDL-C, and

³² See *supra*, note 12.

³³ See *supra*, note 13.

³⁴ See *supra*, note 3.

³⁵ See *supra*, note 28.

particularly the lack of an independent effect of high oleic acid in edible oils (containing at least 70% of oleic acid per serving) on TC and LDL-C levels, FDA has concluded that the evidence provides only qualified support for the scientific validity of the claimed relationship. Therefore, FDA has determined that qualifying language should be included to convey the limits on the strength of the scientific evidence supporting the relationship. FDA thus intends to consider the exercise of its enforcement discretion for a qualified health claim about high oleic acid edible oils (with at least 70% of oleic acid per serving) on the label or in labeling of high oleic acid edible oils that includes a truthful and non-misleading description of the strength of the body of scientific evidence, i.e. “supportive but not conclusive.” Such a description is truthful and not misleading because, while the evidence provides support for the claimed relationship, the evidence is not conclusive. Further, in order for the claim to be truthful and not misleading, the agency will consider, as factors in the exercise of its enforcement discretion, certain other factors discussed below. Based on the above, FDA concludes that there is supportive but not conclusive scientific evidence for a relationship between edible oils, containing at least 70% of oleic acid (MUFA) per serving and reduced risk of CHD, when replaced for greater amounts of SFA.

IV. Other Enforcement Discretion Factors

Factors that FDA intends to consider in the exercise of its enforcement discretion for qualified health claims about oleic acid in edible oils, and edible oil blends, and reduced risk of CHD are discussed below.

A. Qualifying Level of Oleic Acid

The general requirements for health claims provide that, if the claim is about the effects of consuming the substance at other than decreased dietary levels, the level of the substance must be sufficiently high and in an appropriate form to justify the claim. Where no definition for “high” has been established, the claim must specify the daily dietary intake necessary to achieve the claimed effect (21 CFR 101.14(d)(2)(vii)).

The agency determined the minimum effective amount of oleic acid (a MUFA) in high oleic acid oils (with at least 70 % of oleic acid per serving) necessary to be replaced in place of SFAs by first calculating the difference in the amount of oleic acid, in grams, between the high oleic acid oils and high-SFA diets from five controlled studies that demonstrated a reduction in TC and LDL-C (Gillingham et al., 2011; Mata et al., 1997; Kien et al., 2014; Lichtenstein et al., 1993; Zock et al., 1994). The lowest difference that was reported in these studies was used to determine the minimum amount of oleic acid necessary to achieve the relevant benefits. Although, the minimum amount of oleic acid was reported to be lowest in the Lichtenstein et al. (1993) study (about 11 grams of oleic acid per day), the study by Gillingham et al. (2011), with the next lower minimum effective dose, was considered a better representative study for the U.S. population. The Gillingham study included an age group ranging from 18 to 65 years old, while the age range of the subjects in the Lichtenstein study was from 44 to 72 years. Also, the sample size in the Gillingham study (36 males and females) was larger than the Lichtenstein study (15 males and females). For these reasons, the Gillingham study was used to determine the minimum amount of oleic acid consumed per day. Based on our calculation, the minimum amount of oleic acid needed to replace SFA that may result in significant reduction in TC and LDL-C is about 15

grams per day. Consuming about 20 grams of the high oleic acid oils (containing at least 70% of oleic acid per serving) per day provides about 15 grams of oleic acid. Twenty grams of high oleic acid-containing edible oil is about 1½ tablespoons.

To determine the minimum amount of oleic acid in high oleic acid-containing edible oils, or edible oil blends necessary to be eligible to bear the claim, FDA considered a provision of the general requirements for health claims requiring that a health claim enable the public to comprehend the information provided and to understand the relative significance of such information in the context of the total daily diet (see Section 403(r)(3)(B)(iii) of the Act). For health claims, FDA has considered that a typical daily food consumption pattern is composed of 3 meals and a snack or four eating occasions (58 FR 2302-2379; January 6, 1993). Indeed, four eating occasions per day were used to define the qualifying level for three CHD-related health claims: soy protein (64 FR 57700, 57713, October 26, 1999); β-glucan soluble fiber from whole oats (62 FR 3584, 3592, January 23, 1997); and soluble fiber from psyllium seed husks (63 FR 8103, 8109, February 18, 1998). FDA also used this approach to identify 6 grams olive oil, 4.75 grams canola oil, 4.0 grams corn oil per, and 5 grams of soybean oil per Reference Amount Customarily Consumed (RACC) as the qualifying level for products to bear the qualified health claim for these vegetable oils. Consistent with this approach, FDA considered four eating occasions at which consumers might consume high oleic edible oils, or high oleic acid-containing edible oil blends that could potentially be labeled with the requested qualified health claim. The RACC for all oils is one tablespoon.

Based on our calculation, the minimum amount of oleic acid necessary to achieve the relevant benefits, when replacing SFA, is about 15 grams per day. Twenty grams of edible oils that contain at least 70% of oleic acid per serving will provide 15 grams oleic acid per RACC. The RACC for edible oils is one tablespoon. Therefore, to be eligible to bear the high oleic acid edible oils and CHD qualified health claim, the high oleic acid-containing oil, or the high oleic acid-containing edible oil blend, must contain 5 grams of oleic acid per RACC (i.e., $20 \text{ g} \div 4 = 5\text{g}$).

In addition, the agency included phrases in the qualified claims identified below that edible oils containing high oleic acid, consumed at this level, (1) should replace fats and oils higher in saturated fat, and (2) not result in increased caloric intake. The credible evidence that is available, and on which the agency is relying for the qualified claim, suggests that high oleic acid oils may only provide a benefit when used to replace calories and SFA.³⁶ As described above in the “Strength of the Evidence” section, the credible evidence on which the agency is relying reported on comparisons of diets in which the control diets contained amounts of SFA from fats and oils greater than the amounts contained in the high oleic acid oil diets. Although the petitioner requested that the claim language state that the high oleic acid oil replace a “similar

³⁶ The credible evidence that the agency relied on consisted of five intervention studies, which substituted high oleic acid containing oil (at least 70% of oleic acid per serving, or 10 grams of oleic acid per serving) for greater amounts of saturated fat and did not result in increased caloric intake (Gillingham et al., 2011; Mata et al., 1997; Kien et al., 2014; Lichtenstein et al., 1993; Zock et al., 1994). There was no credible scientific evidence available that suggested the reduction in CHD risk could be achieved without replacing high oleic acid oil in the diet for a greater amount of saturated fat. In addition, there was no credible scientific evidence available that suggested the reduction in CHD risk from high oleic acid containing oil consumption could be achieved with increased caloric intake.

amount” of SFA, there was no credible scientific evidence that compared a high oleic acid oil diet to another diet with a similar amount of SFA. In the studies that showed a beneficial effect on CHD, the smallest difference in the amount of SFA between the high oleic acid oil diet and the control diet, was reported as 5.6% of energy (Gillingham et al., 2011). Differences in SFA such as this, when substituted with PUFA and MUFA, can have a significant impact on CHD disease risk.³⁷ As mentioned above, in the section II, the credible scientific evidence indicates that benefits may be realized when a high oleic acid oil in the diet replace fats and oils that are higher in SFA. Furthermore, a claim stating that high oleic acid oils can result in CHD benefits when replacing a “similar amount” of SFA would be misleading because it would suggest that consumers could replace high oleic acid oils with *less* SFA and still achieve the relevant benefits. Such an inference is not supported by the scientific evidence. Therefore, instead of including a phrase that the high oleic acid oils replace a “similar amount” of SFA, we are including the alternative phrasing that makes it clear that oils containing a high level of oleic acid is “to replace fats and oils higher in saturated fat.” This phrasing reflects the state of the science so that consumers can understand the relative significance of the claims in the context of the total daily diet. Similarly, including the phrase that high oleic acid oil is not to “increase the total number of calories you eat in a day” in the qualified health claims also reflects the state of the science, so that consumers can similarly understand the relative significance of the claims in the context of the total daily diet with respect to calories.

Further, the petitioner requested that the claim language include the phrase “edible oil with at least 10 grams of oleic acid *per* serving (one tablespoon)”, to describe the amount of oleic acid needed to make an oil eligible for being considered a high oleic acid oil and necessary to achieve the possible benefit. We have revised the requested claim language to provide greater consumer clarity. The petitioner’s requested language is confusing and misleading to consumers, as they may assume that they should consume 10 grams of oil daily, rather than 20 grams of high oleic acid oil per day, as explained above in this section. Therefore, the phrase “daily intake of about 1½ tablespoons (20 grams) of oils” will be added to the claim, replacing the requested phrasing by the petitioner regarding the amount of oleic acid in a high oleic acid oil. As explained above in this section, based on the evaluation of the credible evidence, consumption of this amount of oil (which provides about 15 grams of oleic acid), may result in a significant reduction in TC and LDL-C when replaced for fats and oils higher in SFA.

Therefore, FDA intends to consider, as a factor in the exercise of its enforcement discretion, the statements that (1) oils containing high levels of oleic acid (a MUFA) should replace fats and oils higher in SFA and (2) consumers are not to increase the total number of calories consumed in a day.

B. Total fat, Saturated Fat, and Cholesterol Criteria for CHD-related Health Claims

³⁷ Furthermore, small differences in saturated fat can have a significant impact on CHD disease risk. For example, a recent report by the American Heart Association demonstrates that replacing 5% of energy intake from saturated fats with equivalent energy intake from polyunsaturated fats and monounsaturated fats was significantly associated with a 25% and 15% lower risk of CHD, respectively (Sacks et al., 2017).

In regulations authorizing CHD-related health claims, FDA has generally required, with a few exceptions, that foods bearing the claims meet the “low fat” criterion defined by 21 CFR 101.62(b)(2), “low saturated fat” criterion defined by 21 CFR 101.62(c)(2), and the “low cholesterol” criterion defined by 21 CFR 101.62(d)(2) (see authorized claims in 21 CFR §§ 101.75, 101.77, 101.81, 101.82, and 101.83). The agency will discuss below how it intends to consider these criteria as factors in deciding whether to exercise its enforcement discretion for a qualified health claim about the relationship between high oleic acid-containing edible oils, or edible oil blends and CHD risk. In section C of this letter, FDA discusses disqualifying levels as defined in 21 CFR 101.14(a)(4) for total fat, saturated fat, cholesterol, and sodium.

“Low fat” criterion

FDA has required in the past that foods bearing CHD-related health claims meet the requirement for “low fat” defined by 21 CFR 101.62(b)(2) as foods that contain less than 3 g of fat per reference amount customarily consumed (RACC), or, for foods with a RACC of less than 30 g or less than 2 tablespoons, per 50 g. The requirement of the “low fat” criterion was first introduced in the dietary lipid and cardiovascular disease proposed rule (56 FR 60727 at 60739; November 27, 1991). FDA stated that, while total fat is not directly related to increased risk for CHD, it may have significant indirect effects. The agency stated that low fat diets facilitate reduction in the intake of SFA and cholesterol to recommended levels. Furthermore, the agency noted that obesity is a major risk factor for CHD, and dietary fats, which have more than twice as many calories per gram as proteins and carbohydrates, are major contributors to total calorie intakes.

There have been several exceptions to this criterion in the past. In the plant sterol/stanol esters and CHD health claim, FDA did not require foods bearing the claim to meet the “low fat” criterion but required that total fat level of foods not exceed the total fat disqualifying level (21 CFR 101.14(a)(4)) with an exception for spreads and dressings for salads, which could not exceed the “low fat” criterion based on the per 50 g basis (21 CFR 101.83(c)(2)(iii)(C)). In not requiring the “low fat” criterion, FDA noted that the Dietary Guidelines for Americans, 2000 (USDA & DHHS, 2000) recommended choosing a diet that is low in SFA and cholesterol and moderate in total fat. Specifically, the Dietary Guidelines for American recommended moderate amounts of foods high in unsaturated fat with a caution to avoid excess calories.

Furthermore, FDA concurs with the current dietary guidelines that continue to note that consuming diets low in SFA is more important in reducing CHD risk than consuming diets low in total fat (DHHS and USDA, 2015-2020).

Edible oils containing at least 70% of oleic acid per serving exceed the “low fat” criterion because they are essentially entirely fat. However, even though these high oleic acid-containing edible oils and edible oil blends do not meet the “low fat” criterion, FDA believes that this type of dietary information will help consumers maintain healthy dietary practices by providing consumers with information that can facilitate reductions of saturated fat and cholesterol intake, while not increasing caloric intake.

Therefore, FDA has decided not to consider, in the exercise of its enforcement discretion, that

edible oils containing at least 70% of oleic acid per serving that bear an oleic acid and CHD qualified health claim meet the “low fat” criterion.

“Low saturated fat” criterion

“Low saturated fat”, as defined by 21 CFR 101.62(c)(2), means that the food must contain less than 1 g of SFA per RACC and not more than 15% of calories from SFA. The RACC for all oils is 1 tablespoon (21 CFR 101.12(b) table 2).

The SFA content of the edible oils containing at least 70% oleic acid per tablespoon identified by the petitioner are described in this paragraph. Per information from USDA National Nutrient Database for Standard Reference Legacy Release, April 2018,³⁸ high oleic acid sunflower oil contains 1.0 g of SFA per tablespoon, and 6.0% of calories from SFA, so it does not meet the first prong of the “low saturated fat” criterion (i.e., food must contain less than 1 g of SFA per RACC); however, it does meet the second prong of the “low saturated fat” criterion (i.e., food must not contain more than 15% of calories from SFA). High oleic acid safflower oil contains slightly more than 1.026 g of SFA per tablespoon, but only 6.7% of calories from SFA, so it does not meet the first prong of the “low saturated fat” criterion; however, it does meet the second prong of the “low saturated fat” criterion. High oleic canola oil contains 0.950 g of SFA per tablespoon and provides 6.0% calories from SFA, so it meets both prongs of the “low saturated fat” criterion. High oleic algal oil contains 0.5 g of SFA and provides 3% calories from SFA, thus meeting both prongs of the “low saturated fat” criterion. Olive oil contains 2 g of SFA per tablespoon and provides more than 15% of calories from SFA and thus does not meet either prong of the “low saturated fat” criterion.

The scientific studies that suggest a relationship between oleic acid in edible oils were used in replacement of edible oils that were high in SFA. The high oleic acid-containing edible oils and CHD qualified health claim will inform consumers that they may lower their risk of CHD by consuming edible oils containing at least 70% of oleic acid per serving instead of oils that contain large amounts of SFA, while not increasing caloric intake. FDA believes this type of dietary information will help consumers maintain healthy dietary practices by providing consumers with information that can facilitate reductions of SFA and cholesterol intake, since these oils contain less SFA than other fat sources. Therefore, FDA has decided not to consider, in the exercise of its enforcement discretion, that high oleic acid-containing edible oils and high oleic acid-containing edible blends containing at least 70% of oleic acid per serving that bear an oleic acid and CHD qualified health claim meet the “low saturated fat” criteria as defined in 21 CFR 101.62(c)(2).

“Low cholesterol” criterion

“Low cholesterol”, as defined by 21 CFR 101.62(d)(2), means that the food contains 20 mg or less of cholesterol per RACC. Like all plant-based foods, most edible oils with at least 70% of

³⁸ The United States Department of Agriculture, National Nutrient Database for Standard Reference 28, does not provide nutrient information on algal oil, but this information was provided by the petitioner.

oleic acid do not contain cholesterol, and therefore, a low cholesterol nutrient content requirement would not limit the use of a high oleic acid containing edible oils and CHD qualified health claim to be used on the label or in the labeling of these oils. There may be edible oil blends with at least 70% of oleic acid that contain non-plant-based ingredients that could cause the product to exceed the “low cholesterol” criterion. Dietary cholesterol is known to increase serum total and LDL-cholesterol levels, which is a risk factor for CHD.

Therefore, FDA intends to consider, in the exercise of its enforcement discretion, that edible oils and edible oil blends with at least 70% of oleic acid that are eligible to bear the oleic acid and CHD qualified health claim must meet the “low cholesterol” criteria as described in 21 CFR 101.62(d)(2).

C. Disqualifying nutrient levels

Under the general requirements for health claims (21 CFR 101.14(e)(3)), a food may not bear a health claim if that food exceeds any of the disqualifying nutrient levels for total fat, SFA, cholesterol, or sodium established in § 101.14(a)(4). Disqualifying total fat levels for individual foods are above 13.0 g per RACC, per label serving size, and, for foods with a RACC of 30 g or less or 2 tablespoons or less, per 50 g. Disqualifying SFA levels for individual foods are above 4.0 g per RACC, per label serving size, and, for foods with a RACC of 30 g or less or 2 tablespoons or less, per 50 g. Disqualifying cholesterol levels for individual foods are above 60 mg per RACC, per label serving size, and, for foods with a RACC of 30 g or less or 2 tablespoons or less, per 50 g. Disqualifying sodium levels for individual foods are above 480 mg per RACC, per label serving size, and, for foods with a RACC of 30 g or less or 2 tablespoons or less, per 50 g.

The general requirements for health claims also provide for FDA to authorize a health claim for a food despite the fact that a nutrient in the food exceeds the disqualifying level, if the agency finds that such a claim will assist consumers in maintaining healthy dietary practices (21 CFR 101.14(e)(3)). In such cases, a disclosure statement that complies with 21 CFR 101.13(h), highlighting the nutrient that exceeds the disqualifying level, would apply.

The application of these regulatory provisions to the oleic acid from edible oils and CHD qualified health claims on high oleic acid-containing edible oils, and high oleic acid-containing edible oil blends are discussed below.

“Total fat” disqualifying level

In the previous section (Section IV, B), FDA explained that the agency has decided not to consider, in the exercise of its enforcement discretion, that edible oils and edible oil blends with at least 70% of oleic acid that bear the oleic acid and CHD qualified health claim meet the “low fat” criteria as defined by 21 CFR 101.62(b)(2). FDA notes, however, that there is a large difference in the amount of total fat between the “low fat” criterion and the “total fat” disqualifying level. For example, the “low fat” criterion for individual foods is equal to or less than 3 g per RACC and per 50 g if the RACC is 30 g or less or 2 tablespoons or less. The

disqualifying “total fat” level for individual foods is above 13 g per RACC, per label serving size and per 50 g if the RACC is 30 g or less or 2 tablespoons or less. Thus, there is a difference of 10 g for individual foods between the “low fat” criterion and the “total fat” disqualifying level.

Edible oils and edible oil blends with at least 70% of oleic acid exceed the disqualifying total fat level because they are essentially entirely fat. However, the edible oils containing at least 70% of oleic acid and CHD qualified health claim will inform consumers that they might lower their risk of CHD by consuming edible oils that contain at least 70% high oleic acid in place of similar foods higher in SFA, while not increasing caloric intake. If FDA did not exempt these oils from the “total fat” disqualifying levels, edible oils with at least 70% of oleic acid, which were included in the scientific studies that suggested a risk reduction relationship, would not be able to bear an oleic acid in edible oils and CHD qualified health claim. FDA believes this type of dietary information will help consumers maintain healthy dietary practices by providing consumers with information that can facilitate reductions of SFA and cholesterol intake without increasing total calorie consumption. In addition, FDA concurs with current Dietary Guidelines for Americans, 2015–2020 that consuming diets low in SFA is more important in reducing CHD risk than consuming diets low in total fat.

Therefore, FDA has decided not to consider, in the exercise of its enforcement discretion that edible oils with at least 70% of oleic acid, and edible oil blends with at least 70% of oleic acid meet the “total fat” disqualifying level to bear the qualified health claim.

“Saturated fat” disqualifying level

In the previous section (Section IV. B), FDA explained that the agency has decided not to consider, in the exercise of its enforcement discretion that edible oils and edible oil blends with at least 70% of oleic acid that bear an oleic acid in edible oils and CHD qualified health claim meet the “low saturated fat” criterion as defined by 21 CFR 101.62(c)(2).

FDA notes that there is a difference in the amount of SFA between the “low saturated fat” criterion and the disqualifying SFA level. For example, the “low saturated fat” criterion for individual foods is equal to or less than 1 g per RACC and less than 15% of the calories from SFA. The disqualifying SFA level for individual foods is above 4 g per RACC, per label serving size and per 50 g. If the food has a RACC of 30 g or less or 2 tablespoons or less, the disqualifying SFA level is above 4g per 50 g. The RACC for olive oil is 1 tablespoon.

Of the edible oils identified in the petition, only olive oil exceeds the “saturated fat” disqualifying level. FDA has already allowed a qualified health claim for “Monounsaturated Fatty Acids From Olive Oil and Coronary Heart Disease” (<http://wayback.archive-it.org/7993/20171114183732/https://www.fda.gov/Food/IngredientsPackagingLabeling/Labeling/Nutrition/ucm072963.htm>). The enforcement discretion letter for the qualified health claim noted that olive oil has 1.8 g of SFA per RACC, and because it has a small RACC (i.e., less than 2 tablespoons) olive oil will exceed the disqualifying saturated fat level based on the 50 gram-criterion (olive oil contains 6.7 g of saturated fat per 50 g (USDA National Nutrient Database for Standard Reference Legacy Release, April 2018)). The general requirements for health claims provide for FDA to authorize a health claim for a food despite the fact that a nutrient in the food

exceeds the disqualifying level, if the agency finds that such a claim will assist consumers in maintaining healthy dietary practices 21 CFR 101.14(e)(3). FDA believes that a qualified health claim about MUFA from olive oil and a reduced risk of CHD would assist consumers in maintaining healthy dietary practices, since the information in the claim informs consumers that replacing SFA in the diet with MUFA from olive oil may reduce the risk of CHD. If FDA did impose the 50 gram-criterion for the “saturated fat” disqualifying level on olive oil, it would prevent this edible oil, which was included in the scientific studies that suggested a relationship, from bearing the claim.

Therefore, FDA has decided not to consider, in the exercise of its enforcement discretion that olive oil with at least 70% of oleic acid, and edible olive oil blends with at least 70% of oleic acid meet the “saturated fat” disqualifying level to be labeled with the qualified health claim.

“Cholesterol” disqualifying level

FDA intends to consider, as a factor in the exercise of its enforcement discretion that edible oils and edible oil blends with at least 70% of oleic acid per serving, as described in section, IV. A and are labeled with an oleic acid and CHD qualified health claim meet the disqualifying cholesterol level as described in 21 CFR 101.14(a)(4).

“Sodium” disqualifying level

FDA intends to consider, as a factor in the exercise of its enforcement discretion that edible oils, and edible oil blends with at least 70% of oleic acid, as described in section, IV. A and are labeled with an oleic acid and CHD qualified health claim meet the disqualifying “sodium” level as described in 21 CFR 101.14(a)(4).

D. 10% minimum nutrient content requirement

Under the general requirements for health claims, a conventional food may not bear a health claim unless it contains, prior to any nutrient addition, at least 10 percent of the DV of vitamin A, vitamin C, iron, calcium, protein, and fiber per reference amount customarily consumed (RACC) (21 CFR 101.14(e)(6)). The purpose of this requirement is to prevent the use of health claims on foods with minimal nutritional value.

For the purposes of this health claim, the agency intends to exercise its enforcement discretion with respect to 21 CFR 101.14(e)(6) for the qualified health claim to be used on food labels when the food contains 10 percent or more of the DV for vitamin D or potassium, in addition to nutrients currently listed (i.e., vitamin A, vitamin C, iron, protein, fiber) per reference amount customarily consumed prior to any nutrient addition.

FDA has previously exempted certain foods from the 10% minimum nutrient content (21 CFR 101.14(e)(6)) when it has been determined that such exemptions could assist consumers in maintaining healthy dietary practices. For example, FDA exempted spreads and dressings for salads from this requirement in the plant sterol/stanol esters and CHD claim interim final rule (65 FR 54686 at 54711, September 8, 2000). FDA also considered a qualified health claim for

walnuts and macadamia nuts and a reduced risk of CHD, even though these nuts did not meet the minimum 10% nutrient requirement (<http://wayback.archive-it.org/7993/20171114183725/https://www.fda.gov/Food/IngredientsPackagingLabeling/LabelingNutrition/ucm072910.htm>) and (<https://www.fda.gov/downloads/Food/LabelingNutrition/UCM568057.pdf>), respectively. In addition, FDA did not consider the 10% minimum nutrient requirement as a factor in the exercise of enforcement discretion for several qualified health claims about other oils, including a qualified health claim about the relationship between “Monounsaturated Fatty Acids From Olive Oil and Coronary Heart Disease”, (<http://wayback.archive-it.org/7993/20171114183732/https://www.fda.gov/Food/IngredientsPackagingLabeling/LabelingNutrition/ucm072963.htm>); “Unsaturated Fatty Acids from Canola Oil and Reduced Risk of Coronary Heart Disease” (<http://wayback.archive-it.org/7993/20171114183734/https://www.fda.gov/Food/IngredientsPackagingLabeling/LabelingNutrition/ucm072958.htm>); “Corn Oil and Corn Oil-Containing Products and a Reduced Risk of Heart Disease” (<http://wayback.archive-it.org/7993/20171114183735/https://www.fda.gov/Food/IngredientsPackagingLabeling/LabelingNutrition/ucm072956.htm>); and “Soybean Oil and Reduced Risk of CHD” (<https://www.fda.gov/downloads/Food/LabelingNutrition/UCM568508.pdf>).

Oleic acid-containing oils and edible oil blends with at least 70% of oleic acid do not meet the 10% minimum nutrient content requirement of 21 CFR 101.14(e)(6). However, edible oils and edible oil blends containing at least 70% of oleic acid per serving can be used in place of SFA in the diet. FDA believes that information to help consumers reduce SFA and cholesterol consumption would assist consumers in maintaining healthy dietary practices. If FDA did impose the 10% minimum nutrient content requirement for oleic acid-containing edible oils and edible oil blends with at least 70% of oleic acid, it would prevent these products from bearing the claim.

Therefore, FDA has decided not to consider, in the exercise of its enforcement discretion that edible oils and edible oil blends containing at least 70% of oleic acid per serving, which bear a high oleic acid and CHD qualified health claim, meet the 10% minimum nutrient content requirement.

V. Conclusions

Based on FDA’s consideration of the scientific evidence submitted with the petition and other pertinent scientific evidence, FDA concludes that there is supportive scientific evidence for a qualified health claim for high oleic acid edible oils and CHD, provided that the qualified health claim is appropriately worded so as not to mislead consumers.

Thus, FDA intends to consider exercising its enforcement discretion for the following qualified health claims:

“Supportive but not conclusive scientific evidence suggests that daily consumption of about 1½ tablespoons (20 grams) of oils containing high levels of oleic acid, when

replaced for fats and oils higher in saturated fat, may reduce the risk of coronary heart disease. To achieve this possible benefit, oleic acid-containing oils should not increase the total number of calories you eat in a day. One serving of [x] oil provides [x] grams of oleic acid (which is [x] grams of monounsaturated fatty acid).”

“Supportive but not conclusive scientific evidence suggests that daily consumption of about 1½ tablespoons (20 grams) of oils containing high levels of oleic acid, may reduce the risk of coronary heart disease. To achieve this possible benefit, oleic acid-containing oils should replace fats and oils higher in saturated fat and not increase the total number of calories you eat in a day. One serving of [x] oil provides [x] grams of oleic acid (which is [x] grams of monounsaturated fatty acid.”

FDA intends to consider exercising its enforcement discretion for the above qualified health claims when all factors for enforcement discretion identified in this letter are met. Qualified health claims on the label or in the labeling of high oleic acid oils are required to meet all applicable statutory and regulatory requirements under the Act, with the exception of the requirement that a health claim meet the significant scientific agreement standard and the requirement that the claim be made in accordance with an authorizing regulation, and any specific exceptions from the general requirements for health claims that has been included in the factors for enforcement discretion identified in this letter. This includes general requirements for health claims in 21 CFR 101.14 (e.g., general requirements set forth in 21 CFR 101.14(e)(3) for disclosure statements that comply with 101.13(h) for saturated fat content, as appropriate).

Please note that scientific information is subject to change, as are consumer consumption patterns. In the event that new information is submitted to the agency, FDA intends to evaluate the new information to determine whether it necessitates a change in this decision. For example, scientific evidence may become available that will support significant scientific agreement.

Sincerely,

Douglas A. Balentine, Ph.D.
Director
Office of Nutrition and Food Labeling
Center for Food Safety
and Applied Nutrition

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