Frito-Lay, Inc.

January 23, 2007

VIA FEDERAL EXPRESS

Division of Nutrition Programs and Labeling
Office of Nutritional Products, Labeling
and Dietary Supplements (HFS-800)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
Harvey W. Wiley Federal Building
5100 Paint Branch Parkway
College Park, MD 20740-3835

Re: Notification for a Health Claim Based on an Authoritative Statement: Unsaturated Fatty Acids from Vegetable Oils and Reduced Risk of Heart Disease

To Whom It May Concern:

Frito-Lay, Inc. submits the enclosed Notification for a Health Claim Based on an Authoritative Statement: Unsaturated Fatty Acids from Vegetable Oils and Reduced Risk of Heart Disease. This notification is submitted pursuant to section 403(r)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 343(r)(3)).

Enclosed you will find two copies of the complete notification including copies of the authoritative documents. Please do not hesitate to contact Dr Kari Hecker Ryan or Dr Bob Brown if you have any questions concerning this submission.

Sincerely,

Kari Hecker Ryan PhD, RD
Manager, Nutrition & Food Safety
Frito-Lay, Inc
972-334-4839

Sincerely,

Bob Brown PhD, MPH
Director, Nutrition & Regulatory
Frito-Lay, Inc.
972-334-4352

Notification for a Health Claim Based on an Authoritative Statement:

UNSATURATED FATTY ACIDS FROM VEGETABLE OILS AND REDUCED RISK OF HEART DISEASE

DATE: **January 23, 2007**

SUBMITTED BY: **Rocco Papalia**
Sr Vice President
Research and Development
Frito-Lay, Inc
7701 Legacy Drive
Plano, TX 75024-4099

SUBMITTED TO: **Division of Nutrition Programs and Labeling**
Office of Nutritional Products, Labeling and Dietary Supplements (HFS-800)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
Harvey W. Wiley Federal Building
5100 Paint Branch Parkway
College Park, MD 20740-3835

TABLE OF CONTENTS

I. INTRODUCTION

Frito-lay, Inc intends to utilize the food label to educate consumers about the heart healthy benefits of substituting monounsaturated (MUFA) and polyunsaturated (PUFA) fats for saturated and trans fats in the diet. Frito-Lay is notifying the Food and Drug Administration (FDA) that it intends to make health claims based upon authoritative statements as required by Section 403(r)(3)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). The health claims will be based on the statements of the following authoritative bodies: the Food and Nutrition Board (FNB) of the National Academy of Sciences (NAS); the Institute of Medicine (IOM) of the NAS; the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) organized by the National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH); Healthy People 2010 co-lead by the FDA and the NIH; and the 2005 Dietary Guidelines for Americans (Department of Health and Human Services (HHS) and the Department of Agriculture (USDA)). Frito-Lay intends to use three health claims found equally understandable by consumers, based on scientifically valid consumer research:

1. ***Replacing saturated and trans fats like butter and shortenings with similar amounts of unsaturated fats from vegetable oils like [name of oil] may reduce the risk of heart disease. To achieve this benefit, total daily calories should not increase.***

Or

2. ***Unsaturated fats in vegetable oils such as [name of oil] may reduce the risk of heart disease when they replace similar amounts of saturated and trans fats in the diet. To achieve this benefit, total daily calories should not increase.***

Or

3. ***Replacing saturated and trans fats with similar amounts of unsaturated fats from vegetable oils such as [name of oil], may reduce the risk of heart disease. To achieve this benefit, total daily calories should not increase.***

The claims will apply to essentially pure vegetable oils, spreads and shortenings that have a total unsaturated fat content of 80% or more and saturated fat content no more than 20% of total fat, which translates to an unsaturated to saturated fat ratio greater than or equal to 4:1. The claims will also apply to eligible oil-containing foods in the following categories only: crackers, salad dressings (including mayonnaise and mayonnaise-type dressings), salads (including cabbage salad and other coleslaw-type products), sauces and dips (including tarter sauce) and grain, vegetable and fruit-based snacks. Eligibility criteria for the health claims are as follows: oils, spreads, shortenings and oil-containing foods must contain a minimum of 4.5 grams of total unsaturated fats derived from an eligible vegetable oil per RACC. When total fat content in oil-containing foods exceeds the disqualifying levels as defined by 21 CFR §101.14(a)(4) packaging must include the disclosure statement required by 21 CFR §101.13(h). Saturated fat content must not exceed 20 percent of total fat content to maintain a 4 to 1 ratio of unsaturated to saturated fats. The disqualifier level for this dietary constituent would apply to oil-containing foods. Pure vegetable oils, spreads and shortenings (products that are largely composed of oil) will be exempt from the 50 gram criterion of the saturated fat disqualifier level. Oils, spreads, shortenings and oil-containing foods must comply with disqualifying levels for sodium; be eligible to bear a declaration of 0 grams of

trans fat (i.e., <0.5 g/serving); and meet the definition of low cholesterol (21 CFR §101.62(d)).

II. AUTHORITATIVE STATEMENTS

The FDA Modernization Act of 1997 (FDAMA) permits claims based on current, published authoritative statements from "a scientific body of the United States with official responsibility for public health protection or research directly related to human nutrition . . . or the National Academy of Sciences (NAS) or any of its subdivisions." [1]

The proposed claims are based on the following authoritative statements which, collectively, serve to demonstrate the significant scientific consensus regarding the relationship between unsaturated fats and reduced risk of heart disease.

A. Diet and Health: Implications for Reducing Chronic Disease Risk (1989)[2]

1. *"Clinical and animal studies provide firm evidence that omega-6 polyunsaturated fatty acids when substituted for saturated fatty acids result in a lowering of serum total cholesterol and LDL cholesterol and usually also some lowering of HDL cholesterol levels." [Page 8]*

2. *"Clinical studies indicate that substitution of monounsaturated for saturated fatty acids results in a reduction of serum total cholesterol and LDL cholesterol without a reduction in HDL cholesterol." [Page 8]*

B. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids – DRI Macronutrient Report (2002)[3]

3. *"Monounsaturated and polyunsaturated fatty acids reduce blood cholesterol concentration and help lower the risk of heart disease when they replace saturated fatty acids in the diet.".[Report Brief[4],Page 4]*

---

[1] Guidance for Industry: Notification of a Health Claim or Nutrient Content Claim Based on an Authoritative Statement of a Scientific Body
[2] FNB, NAS
[3] IOM, NAS

4. Interventional Evidence: *"…in weight-stable individuals, a high monounsaturated fatty acid, low saturated fatty acid diet results in a more favorable metabolic profile with respect to total cholesterol, HDL cholesterol, and triacylglycerol concentrations."*[5] *[Page 818].*

5. Epidemiological evidence: *"…high intakes of n-6 polyunsaturated fats have been associated with blood lipid profiles (e.g., reduced total and low density lipoprotein [LDL] cholesterol, reduced triacylglycerol, and increased high density lipoprotein [HDL] cholesterol concentrations) that are associated with low risk of coronary heart disease." [Page 820].*

6. Interventional Evidence: *"From the standpoint of blood lipid concentration and CHD, higher* n-*6 polyunsaturated fatty acid intake generally alters blood lipid concentration to result in a decreased risk profile. Controlled trials have examined the effects of substituting* n-*6 fatty acids in the diet to replace carbohydrate or saturated fatty acids. In general, any fat that replaces carbohydrate in the diet raises HDL cholesterol and decreases triacylglycerol concentrations, with only small differences between individual fatty acids.* n-*6 Fatty acids decrease LDL cholesterol concentrations to a much greater degree than do saturated fatty acids." [Page 821]*

C. Healthy People 2010 (2000)[6]

7. *"Saturated fatty acids are the major dietary factors that raise blood low-density lipoprotein (LDL) cholesterol levels, increasing the risk for heart disease. Increasing evidence suggests that trans-fatty acids also can increase LDL-cholesterol levels. Monounsaturated and polyunsaturated fatty acids do not raise blood cholesterol." [Page 19-29]*

8. *"Substituting monounsaturated and polyunsaturated fatty acids for saturated fatty acids can help lower health risks." [Page 19-30]*

D. Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Full Report (2002)

---

[4] Shaping the Future for Health, Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids, 2002.
[5] MUFA vs low fat diet where MUFA replaced saturated fat in the diet
[6] U.S. Department of Health and Human Services. Healthy People 2010: Understanding and Improving Health. 2nd ed. Washington, DC: U.S. Government Printing Office, November 2000.

Evidence Statements

9. *"Monounsaturated fatty acids lower LDL cholesterol relative to saturated fatty acids (A2, B2[7],[8]). Monounsaturated fatty acids do not lower HDL cholesterol nor raise triglycerides (A2, B2)." [Page V-10]*

10. *"Linoleic acid, a polyunsaturated fatty acid, reduces LDL cholesterol levels when substituted for saturated fatty acids in the diet (A1, B1)." [Page V-11]*

11. *"Controlled clinical trials indicate that substitution of polyunsaturated fatty acids for saturated fatty acids reduces the risk of CHD (A2, B2)." [Page V-11]*

12. ***"Recommendation**: Intakes of trans fatty acids should be kept low. The use of liquid vegetable oil, soft margarine, and trans fatty acid-free margarine are encouraged instead of butter, stick margarine, and shortening." [page V-9]*

E. 2005 Dietary Guidelines – Key Recommendations (2005)[9]

13. *"Keep total fat intake between 20 to 35 percent of calories, with most fats coming from sources of polyunsaturated and monounsaturated fatty acids, such as fish, nuts, and vegetable oils."* [page viii]

14. *"Limit intake of fats and oils high in saturated and/or* trans *fatty acids, and choose products low in such fats and oils."* [page viii]

The authoritative statements are provided in Appendices A – G.

III. AUTHORITATIVE STATUS OF THE STATEMENTS

The 14 statements presented above qualify as authoritative statements under section 403(r)(3)(C) of the FD&C Act. In each case, the statement involves the

[7] National Cholesterol Education Program National Heart, Lung, and Blood Institute. National Institutes of Health. NIH Publication No. 02-5215. September 2002.
[8] **Type of Evidence:** A: Major randomized controlled clinical trials (RCTs), B: Smaller RCTs and meta-analyses of other clinical trials, C: Observational and metabolic studies, D: Clinical experience. **Strength of Evidence** 1: Very strong evidence, 2: Moderately strong evidence, 3 Strong trend
[9] *Dietary Guidelines for Americans 2005*. Released January 12, 2005, by HHS Secretary Tommy G. Thompson and USDA Secretary Ann M. Veneman.

relationship between the replacement of saturated fats with unsaturated fats and coronary heart disease (CHD) or its surrogate biomarkers (total and LDL cholesterol levels). None of the statements were by an employee of the scientific body made in an individual capacity. All statements appear in documents "published by a subdivision of one of the Federal scientific bodies" including executive summaries (statements 1- 3, 13 - 14) or relevant chapters in reports that conducted "deliberative reviews by the scientific body of the scientific evidence" to summarize current science and provide recommendations for dietary intakes to reduce the risk of disease (statements 4-12) and which ultimately serve to influence public health and regulatory policy. The proposed statements were published between 1989 and 2005, demonstrating that these authoritative statements on the relationship between unsaturated fats and CHD are currently in effect as required. Several studies have subsequently been published on this diet-disease relationship, which further support these authoritative statements. These studies are summarized elsewhere in this notification.

Frito-Lay believes there is strong precedent that establishes the sources of the proposed authoritative statements cited above for this purpose under FDAMA. Specifically:

- Statements from *Diet and Health* have been used to establish FDAMA health claims for whole grains and coronary heart disease (1999[10] and 2003[11]) and potassium and blood pressure and stroke (2000)[12].

[10] http://www.cfsan.fda.gov/~dms/flgrains.html
[11] http://www.cfsan.fda.gov/~dms/flgrain2.html

- Statements from the IOM DRI Macronutrient Report (Ch 1, 8, and 11) were deemed "authoritative" in all three FDAMA nutrient content claim notifications for omega-3 fatty acids (FDA Docket Nos. 2004N-0217, 2005P-0189, 2006P-0137).
- The National Cholesterol Education Program Adult Treatment Panel (III) Report was recognized as an authoritative document for the 2006 FDAMA health claim regarding saturated fat, cholesterol, and trans fat, and reduced risk of heart disease[13]. The statements from this report indicate the evidence that unsaturated fats reduce the risk of heart disease when they replace saturated fat is moderately to very strong. It clearly states that vegetable oils should be used instead of butter, stick margarines and shortenings to keep saturated and trans fat intakes as low as possible.
- Statements from the 2005 Dietary Guidelines for Americans are taken from the Key Recommendations in the executive summary. The Key Recommendations are considered authoritative according to the statements in the Executive Summary (page vii) and the 2006 FDAMA health claim regarding saturated fat, cholesterol, and trans fat, and reduced risk of heart disease. The Key Recommendations in the 2005 Dietary Guidelines explicitly state types of fatty acids and oils to consume or avoid as part of a healthy diet to reduce chronic disease. The first statement serves to identify that most dietary fat sources should be MUFA and PUFA from vegetable oils (the premise of the proposed health claims) as well as fish and nuts. The second statement serves to

[12] http://www.cfsan.fda.gov/~dms/hclm-k.html
[13] http://www.cfsan.fda.gov/~dms/flfats.html

emphasize that a healthy diet should keep saturated and trans fat as low as possible and that foods low in these types of fats or oils should be chosen.

- The statements included from Healthy People 2010 fulfill the requirements for authoritative statements in that they are (1) within the federal agencies identified as authoritative bodies, including the Department of Health and Human Services and the NIH-NHLBI; (2) the statements specifically link unsaturated fats to reduced blood cholesterol levels and health risks and; (3) the statements are not qualified with recommendations for future research or suggestions that they are based on inconclusive or preliminary data.

In conclusion, it is the position of Frito-Lay that all presented authoritative statements meet the requirements for health claims based on authoritative statements under Section 403(r)(3)(C) of the FD&C Act and serve to demonstrate overwhelming consensus on the relationship between unsaturated fats and reduced risk of heart disease.

IV. FDA ADVISORY OPINION

Further support of the relationship between unsaturated fat and reduced risk of heart disease was furnished by the estimated benefits of trans fat labeling provided by FDA in its proposed and final rules on this topic[14]. While these documents are not authoritative statements under FDAMA, they are official FDA advisory opinions on the role of fats in heart health and are, therefore, germane to this notification.

[14] 64 FR 62745, November 17, 1999. Food Labeling: Trans Fatty Acids in Nutrition Labeling, Nutrient Content Claims, and Health Claims; Proposed Rule.
68 FR 41434, July 11, 2003. Food Labeling; Trans Fatty Acids in Nutrition Labeling; Consumer Research to Consider Nutrient Content and Health Claims and Possible Footnote or Disclosure Statements; Final Rule and Proposed Rule

FDA used a three-prong approach to estimate the benefit of its proposed trans fat labeling regulations: (1) The changes in trans fat intake that would result from labeling changes; (2) the changes in health states that would result from changes in trans fat intakes; and (3) the value of changes in health states in terms of life-years gained, number of cases or deaths avoided and the dollar value of such benefits. For changes in health states two methods were used to estimate the potential decrease in CHD likely to result from decreased intake of trans fat in response to the labeling change:

- Method 1. Decrease in CHD risk due to decreased serum concentrations of LDL–C.
- Method 2. Decrease in CHD risk due to decreased serum concentrations of LDL–C and increased concentrations of HDL-C.

The primary assumption in this analysis was that trans fat would be replaced by unsaturated fats, carbohydrates, or a combination of unsaturated and saturated fats. **Table 1** from the final rule (64 FR 41434 at 41481) shows the negative consequences of replacement of other fatty acids and carbohydrates with trans fats on blood lipid levels. **Table 2** (64 FR 41434 at 41481) shows the changes in CHD risk as indicated by LDL and HDL cholesterol concentrations. The greatest reduction in CHD risk is associated with a 0.1 percent replacement of trans fat with PUFA. However, replacement of 0.1 percent of energy from trans fat with a combination of MUFA and PUFA incurs a nearly identical reduction in CHD risk. Based on Method 2, replacement of trans fat with carbohydrate reduces CHD risk half as much as the isocaloric substitution of the combination of unsaturated fats.

Table 3 (64 FR 41434 at 41487) of the final rule, shows the predicted changes in CHD risk expected three years after the effective date for trans fat labeling. FDA used the three most likely macronutrient substitutions to predict CHD risk reduction, which included (1) 100 percent cis-monounsaturated fat, (2) a mixture of 50 percent cis-monounsaturated and 50 percent cis-polyunsaturated fat, or (3) a mixture of 50 percent cis-monounsaturated and 50 percent saturated fat. Using a probabilistic model, CHD risk is predicted to be reduced by 0.052 to 0.106 percent three years after trans fat labeling goes into effect.

Table 1. SUMMARY OF CHANGES IN SERUM LIPIDS AND CHD RISK WITH DIFFERENT MACRONUTRIENT SUBSTITUTIONS - CHANGE IN SERUM LIPIDS WITH SUBSTITUTION OF Trans FATTY ACIDS FOR DIFFERENT TYPES OF FATTY ACIDS OR CARBOHYDRATE (Source: 68 FR 41433 at 41481)

Macronutrient	*Cis*-monounsaturated Fatty Acid	*Cis*-polyunsaturated Fatty Acid	Saturated Fatty Acid	Carbohydrate	Half *cis*-monounsaturated and half *cis*-polyunsaturated	Half *cis*-monounsaturated and half saturated	Half *cis*-monounsaturated and half carbohydrate
Change in Serum Lipid When Replaced by *Trans* Fat	mg/dL per 1% of energy	mg/dL per 1% of energy	mg/dL per 1% of energy	mg/dL per 1% of energy	mg/dL per 1% of energy	mg/dL per 1% of energy	mg/dL per 1% of energy
LDL	1.5	1.81	-0.02	1.26	1.66	0.74	1.38
HDL	-0.4	-0.34	-0.53	-0.06	-0.37	-0.47	-0.23

Table 2. SUMMARY OF CHANGES IN SERUM LIPIDS AND CHD RISK WITH DIFFERENT MACRONUTRIENT SUBSTITUTIONS - CHANGE IN CHD RISK WITH REPLACEMENT OF Trans FATTY ACIDS BY DIFFERENT TYPES OF FATTY ACIDS OR CARBOHYDRATE (Source: 68 FR 41433 at 41481)

Macronutrient	*Cis*-monounsaturated Fatty Acid	*Cis*-polyunsaturated Fatty Acid	Saturated Fatty Acid	Carbohydrate	Half *cis*-monounsaturated and half *cis*-polyunsaturated	Half *cis*-monounsaturated and half saturated	Half *cis*-monounsaturated and half carbohydrate
Change in CDH Risk With Replacment of *Trans* Fat	Percent per 0.1% of energy	Percent per 0.1% of energy	Percent per 0.1% of energy	Percent per 0.1% of energy	Percent per 0.1% of energy	Percent per 0.1% of energy	Percent per 0.1% of energy
Method 1, LDL	-0.147	-0.177	0.002	-0.123	-0.162	-0.073	-0.135
HDL	-0.140	-0.119	-0.186	-0.021	-0.130	-0.163	-0.081
Method 2, LDL + HDL	-0.287	-0.296	-0.184	-0.144	-0.292	-0.235	-0.216

Table 3. PREDICTED CHANGES IN CHD RISK DUE TO Trans FAT LABELING ACCORDING TO MACRONUTRIENT SUBSTITUTION FOR Trans FAT (Source: (Source: 68 FR 41433 at 41487)

Time after Effective Date for Final Rule[1]	Decrease in *Trans* Fat Intake (% of Energy)	Source of Decrease	Substitution for *Trans* Fat	Percent Decrease in CHD Risk		
				Method 1, LDL	HDL	Method 2, LDL and HDL
3 years	0.0378	Consumer choice and margarine reformulation	mono	-0.056%	-0.053%	-0.108%
			mono+ poly	-0.061%	-0.049%	-0.110%
			mono+ sat	-0.027%	-0.062%	-0.090%
			Substitution from probabilistic model.	-0.052%	-0.054%	-0.106%

[1] The time after the effective date for the final rule includes 3 years for decreases in *trans* fat intake to result in changes in CHD risk.

In summary, several key messages can be taken from the trans fat labeling regulations. First, the health benefit calculations showed that substituting trans fats with unsaturated fats will incur the greatest reduction in CHD risk compared with carbohydrate and saturated fat. Second, the predicted changes in CHD risk were based on what the FDA considered the most likely substitutions which included other fatty acids rather than carbohydrate. Third, the predicted changes in CHD risk were not subject to additional nutritional criteria; namely reductions in total fat or minimum nutrient requirements. Thus, the position adopted by FDA is that the reduction in CHD risk is solely a factor of fatty acid substitution. MUFA and PUFA are heart healthy because they reduce total and LDL cholesterol levels and increase HDL levels when they replace trans fats in the diet. The absence or presence of other nutrients was not considered important in this context. Therefore, the agency took the position that the 10% DV minimum nutrient content provision of the general health claim requirements (21 CFR § 101.14(e)(6)) need not apply for reduced CHD risk, though fatty acid substitutions should be made within the context of an overall healthy diet to optimize the reduction of the risk of chronic diseases.

The reduction of trans fats in margarines was primarily used by FDA to estimate CHD risk predictions in the proposed rule for this initiative, but, “consumer choice” was also considered. Trans fats are found in a variety of foods including margarines. It is therefore likely that the benefits of trans fat labeling will be greater than predicted because other food categories are being reformulated to reduce or eliminate trans fatty acids. Consumer choice will be a crucial factor in realizing the potential health benefits of these regulations considering the large array of potentially trans fat–reduced foods available. Therefore, in conjunction with mandatory trans fat labeling, the proposed health claim for unsaturated fats and CHD will provide consumers with better information to help maintain healthy dietary practices and food manufacturers with powerful incentives to replace trans fat-containing oils with unsaturated fatty acid-predominant alternatives rather than those high in saturated fat sources. FDA clearly expressed a preference for such oils in the preamble to the final rule, “The inclusion of [saturated fat] does not indicate that FDA projects that trans fat will be replaced by 100 percent saturated fat, or that FDA would encourage such an inappropriate substitution.” (68 FR 41434 at 41481)

In conclusion, FDA’s trans fat rulemaking provides strong support for the proposed claims because they would provide consumers with information needed to make informed dietary choices and would provide food manufacturers with strong incentives to use alternative sources of fat that are predominant in unsaturated fatty acids. These rules also indicate that reduced risk of CHD would arise from changes in fatty acid intake and not other nutrients. Therefore, the 10% DV minimum nutrient

content requirement should not apply. Additional thoughts on this subject are presented in later sections of this notification.

V. CONTENT OF THE FDAMA NOTIFICATION

The proposed health claims meet all other FDAMA requirements in that they are accurate representations of the authoritative statements, they enable the public to comprehend the information, and the information is presented in the context of the total daily diet. The proposed health claims are truthful and not misleading. The proposed claims meet the burden of significant scientific agreement in that qualified experts (members on the committees of the Federal authoritative bodies) agree that sound science supports the claims. Finally, though qualified health claims exists for monounsaturated fats from olive oil and unsaturated fats from canola oil and reduced risk of CHD, the proposed health claims are uniquely different because they apply to MUFA and PUFA **and** are not specific to one type of oil. The proposed claims are consistent with the recommendations from the 2005 Dietary Guidelines for Americans that "most fats should come from monounsaturated and polyunsaturated sources," which includes a variety of vegetable oils.

VI. EXACT WORDING OF THE PROPOSED CLAIM

1. ***Replacing saturated and trans fats like butter and shortenings[15] with similar amounts of unsaturated fats[16] from vegetable oils like [name of oil] may reduce the risk of heart disease. To achieve this benefit, total daily calories should not increase.***

Or

[15] May also include tropical oils such as coconut, palm, or palm kernel oils.
[16] Monounsaturated and polyunsaturated fats may replace unsaturated fats if desired.

2. ***Unsaturated fats in vegetable oils such as [name of oil] may reduce the risk of heart disease when they replace similar amounts of saturated and trans fats in the diet. To achieve this benefit, total daily calories should not increase.***

Or

3. ***Replacing saturated and trans fats with similar amounts of unsaturated fats from vegetable oils such as [name of oil], may reduce the risk of heart disease. To achieve this benefit, total daily calories should not increase.***

All three of the proposed health claims accurately reflect the authoritative statements within the context of the total diet. Scientifically valid consumer research showed that these claims are clear and understandable. Frito-Lay believes that all three statements are equally understandable health claims to communicate the heart health benefits of unsaturated fats. Consumer research that documents the effectiveness of the proposed claims is provided in Appendix H.

VII. STATUTORY BASIS FOR A HEALTH CLAIM BASED ON AUTHORITATIVE STATEMENTS

Section 403(r)(3) of the FD&C Act, as added by FDAMA authorizes food manufacturers to make health claims based on authoritative statements from an identified authoritative body such as the NAS and NIH.

REQUIREMENTS

Health claims based on authoritative statements are authorized for use provided the following conditions and criteria are met:

> (3)(A) Except as provided in subparagraph (5), a claim described in subparagraph (1)(B) may only be made -
>
> (i) if the claim meets the requirements of the regulations of

the Secretary promulgated under clause (B), and

(ii) if the food for which the claim is made does not contain, as determined by the Secretary by regulation, any nutrient in an amount which increases to persons in the general population the risk of a disease or health-related condition which is diet related, taking into account the significance of the food in the total daily diet, except that the Secretary may by regulation permit such a claim based on a finding that such a claim would assist consumers in maintaining healthy dietary practices and based on a requirement that the label contain a disclosure of the type required by subparagraph (2)(B). (B)(i) The Secretary shall promulgate regulations authorizing claims of the type described in subparagraph (1)(B) only if the Secretary determines, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence.

(ii) A regulation described in subclause (i) shall describe - (I) the relationship between a nutrient of the type required in the label or labeling of food by paragraph (q)(1) or (q)(2) and a disease or health-related condition, and

(II) the significance of each such nutrient in affecting such disease or health-related condition.

(iii) A regulation described in subclause (i) shall require such claim to be stated in a manner so that the claim is an accurate representation of the matters set out in subclause (ii) and so that the claim enables the public to comprehend the information provided in the claim and to understand the relative significance of such information in the context of a total daily diet.

(C) Notwithstanding the provisions of clauses (A)(i) and (B), a claim of the type described in subparagraph (1)(B) which is not authorized by the Secretary in a regulation promulgated in accordance with clause (B) shall be authorized and may be made with respect to a food if -

(i) a scientific body of the United States Government with official responsibility for public health protection or research directly relating to human nutrition (such as the National Institutes of Health or the Centers for Disease Control and Prevention) or the National Academy of Sciences or any of its subdivisions has published an authoritative statement, which is currently in effect, about the relationship between a nutrient and a disease or health-related condition to which the claim refers;

(ii) a person has submitted to the Secretary, at least 120 days (during which the Secretary may notify any person who is making a claim as authorized by clause (C) that such person has not submitted all the information required by such clause) before the first introduction into interstate commerce of the food

with a label containing the claim, (I) a notice of the claim, which shall include the exact words used in the claim and shall include a concise description of the basis upon which such person relied for determining that the requirements of subclause (i) have been satisfied, (II) a copy of the statement referred to in subclause (i) upon which such person relied in making the claim, and (III) a balanced representation of the scientific literature relating to the relationship between a nutrient and a disease or health-related condition to which the claim refers;

(iii) the claim and the food for which the claim is made are in compliance with clause (A)(ii) and are otherwise in compliance with paragraph (a) and section 321(n) of this title; and

(iv) the claim is stated in a manner so that the claim is an accurate representation of the authoritative statement referred to in subclause (i) and so that the claim enables the public to comprehend the information provided in the claim and to understand the relative significance of such information in the context of a total daily diet. For purposes of this clause, a statement shall be regarded as an authoritative statement of a scientific body described in subclause (i) only if the statement is published by the scientific body and shall not include a statement of an employee of the scientific body made in the individual capacity of the employee.

(D) A claim submitted under the requirements of clause (C) may be made until -

(i) such time as the Secretary issues a regulation under the standard in clause (B)(i) - (I) prohibiting or modifying the claim and the regulation has become effective, or (II) finding that the requirements of clause (C) have not been met, including finding that the petitioner has not submitted all the information required by such clause; or (ii) a district court of the United States in an enforcement proceeding under subchapter III of this chapter has determined that the requirements of clause (C) have not been met.

Frito-Lay concludes that the proposed health claims meet these requirements and have the potential to improve public health by assisting consumers to make healthy dietary choices consistent with dietary guidance from the authoritative bodies cited previously.

VIII. MINIMUM EFFECTIVE AMOUNT OF TOTAL UNSATURATED FATS

The minimum effective amount of total unsaturated fat content was determined according to the calculations described in the FDA response letter to the qualified health claim for unsaturated fatty acids from canola oil and CHD (the Canola Oil QHC)[17] and would also serve as marker for compliance for the present health claim. In the present case, it is proposed that the minimum amount of unsaturated fats

[17] http://www.cfsan.fda.gov/~dms/qhccanol.html

should be based on the eligible heart healthy vegetable oils with the highest saturated fat content to ensure that all eligible oils would provide health benefits when substituted for saturated and trans fats.

According to the USDA National Nutrient Database for Standard Reference (Release, 19) olive, soybean, and peanut oils have the highest saturated fat content (13.8%, 14.4%, 16.9% energy, respectively) of oils recommended for consumption by authoritative bodies. Sesame oil has similar saturated fat content, but was not considered in these calculations due to its low use by consumers (ERS Oil Crops Yearbook 2005) and limited scientific data regarding minimum effective dose. Based on the approach FDA took in the Canola Oil QHC, we utilized data from randomized, controlled-feeding studies that demonstrated the lowest effective dose of total unsaturated fatty acids required to lower total- and LDL-cholesterol levels compared to higher saturated fat diets while keeping total fat intake constant (Mata et al, 1992; Kris-Etherton et al, 1999; Baudet 1988, Lichtenstein et al, 1999; Vega-Lopez et al, 2006). A summary of these studies is presented in **Table 4** and brief descriptions of the studies are presented in **Table 5**. Appropriately, the predominant fatty acid in olive oil is MUFA (oleic acid), the predominant fatty acid in soybean oil is PUFA (linoleic [~8% alpha-linolenic]), and peanut oil contains significant amounts of both MUFA and PUFA.

TABLE 4. Difference Between UFA Intakes and Serum Lipids in Six Well-Controlled Studies Used to Calculate the Minimum Effective Dose for Unsaturated Fats (versus saturated fats)					
Reference	Oil Type	Δ UFAs (% en)	Δ UFAs (g/ 2000 kcal)	Δ TC (%)	Δ LDL (%)
Mata et al (1992)	Olive oil	8.0	17.8	-8.9	-17.6
Kris-Etherton et al (1999)	Olive Oil	9.0	20.0	-11.5	-15.3
Lichtenstein et al (1999)	Soybean Oil	10	22.5	-10.4	-13.0
Vega-Lopez et al (2006)	Soybean Oil	6.2	13.8	-8.3	-12.1
Kris-Etherton et al (1999)	Peanut Oil	8.0	17.8	-8.9	-11.1
Baudet et al (1988)	Peanut Oil	7.3	16.2	-8.1	-8.8
Mean		8.1	**18.0**	-9.3	-13.0

TABLE 5. Description of the Studies Used to Calculate the Minimum Effective Dose for Unsaturated Fats					
Reference	Study Design	# Subjects	Serum cholesterol levels (mg/dl)	Duration of diets	Diet Description
Mata et al (1992)	3 period, cross-over	21 women	TC < 240	4 wk SFA diet; 6 week MUFA diet	SFA diet (palm and butter): 44% CHO, 40% fat.. OO diet 49% CHO, 35% fat (1/2 OO)
Kris-Etherton et al (1999)	RCT; 5 period cross-over	9 men; 13 women	TC 188; LDL 118	24 d	AAD and test diets 50% CHO; ~34% fat (1/2 from OO, peanut oil or mixed fats)
Lichtenstein et al (1999)	RCT; 6 period cross-over	18 women; 18 men	LDL > 130	35 d	All diets ~55% CHO; 30% fat (2/3 from soy oil or butter)
Vega-Lopez et al (2006)	RCT; 4 period cross-over	5 men; 10 women	LDL > 130	35 d	All diets ~55% CHO; 30% fat (2/3 palm or soy oils)
Baudet et al (1988)	RCT; 4 period cross-over	20 women	TC 208	6 weeks	All diets 54% CHO, 30% fat; (15.6% from peanut oil or milk fat)

The data in Table 4 show that the mean amount of unsaturated fatty acids (UFAs) that resulted in a significant decrease in total- and LDL-cholesterol (LDL-C) when substituted for saturated fats was 18.0 grams per day. Frito-Lay intends to use this value as the minimum effective dose for the new claims. Based on a dietary pattern of three meals and one snack per day, as utilized in the Canola and Olive Oil QHCs, the minimum effective amount of total unsaturated fats necessary to be in a food was determined to be 4.5 grams per RACC. Because the unsaturated fat (and saturated fat) content varies between healthy oils, the total minimum gram amount of oil necessary for oil-containing foods will range between 5 and 6 grams per RACC. For example, to achieve 4.5 grams of unsaturated fat in a food, 5 grams of canola oil would be required per RACC. However, because peanut oil contains more saturated fat, 6 grams would be required to achieve 4.5 g of unsaturated fat per RACC.

The fatty acid content of foods must be analytically determined pursuant to 21 CFR §101.9(g). Accordingly, the "Official Methods of Analysis of AOAC International," 15th ed (1990) should be used, and if no AOAC method is available or appropriate, other reliable and appropriate analytical procedures may be used. For use of the proposed health claims, the content of unsaturated fats, saturated fat, trans fat, cholesterol, and sodium must be based on analytical methods as product eligibility would not be based on rounded values.

Frito-Lay concludes that the criteria proposed herein would enable consumers to make healthy choices regarding oils and oil-containing foods while keeping saturated and trans fat and cholesterol intakes as low as possible and within total fat recommendations. The minimum effective amount of unsaturated fats is appropriate because the clinical trials included to determine the effective amount were well designed and controlled and kept total fat intake constant between diets, thus establishing a causative relationship between types of fatty acids and serum lipid levels. Finally, the reductions in total and LDL cholesterol levels were clinically significant in all studies, ranging from 9 to 11 percent for total cholesterol and 9 to 18 percent for LDL cholesterol. FDA has not provided specific criteria on the minimum reduction in total cholesterol and/or LDL cholesterol it considers necessary to warrant authorization of a claim. However a decrease in total cholesterol of 4.4 percent (10.0 milligrams mg/dL) and in LDL-cholesterol of 4.9 percent (7.8 mg/dL) was regarded as significant in authorizing a health claim for oats and coronary heart disease (62 FR 3584, 3586, January 23, 1997), and similar levels were used to justify authorizing the health claim for soy protein and CHD (64 FR 57700, 57708, October 26, 1999).

IX. NATURE OF FOODS ELIGIBLE TO BEAR THE CLAIM

The DRI Macronutrient Report (2002) specifically indicates that low saturated fat vegetable oils contain 20 percent saturated fat or less. The report states that should all dietary fats consumed be low in saturated fat (i.e., 20 percent of fat energy), a

total fat intake of 35 percent of total energy would result in a saturated fat intake of 7 percent of calories (page 799). Based on this statement it was determined that a heart healthy oil would be classified as providing no more than 20 percent of total fat content from saturated fat and would require a minimum of 80 percent fat content as MUFA and PUFA combined. For descriptive purposes this approach equates to an unsaturated to saturated fat ratio of greater than or equal to 4 to 1.

Vegetable Oils, Spreads, & Shortenings: Vegetable oils, spreads and shortenings (that are composed primarily of the vegetable oils) eligible for the proposed health claims would be identified by a total unsaturated fat to saturated fat ratio of greater than or equal to 4:1. Similar to the Olive Oil QHC[18], the total fat disqualifying level would not apply and the saturated fat content would not be permitted to exceed 4 grams per RACC but would be exempt from the 50 gram criterion for small serving sizes of this disqualifier level according to 21 CFR §101.14(a)(4). All other eligibility criteria would be the same as for oil-containing foods which are outlined below.

Oils eligible for the proposed claim are listed in **Table 6**. These oils have been recommended by several authoritative sources as healthy oils because of their favorable ratio of unsaturated to saturated fat content including the 2005 Dietary Guidelines for Americans, Healthy People 2010 and the National Cholesterol Education Program (NCEP) of the National Heart, Lung and Blood Institute. Recommendations from the NCEP (**Figure 1**) are particularly noteworthy This "Tip Sheet: Fats and Oils to Choose" designates oils that would qualify for the proposed

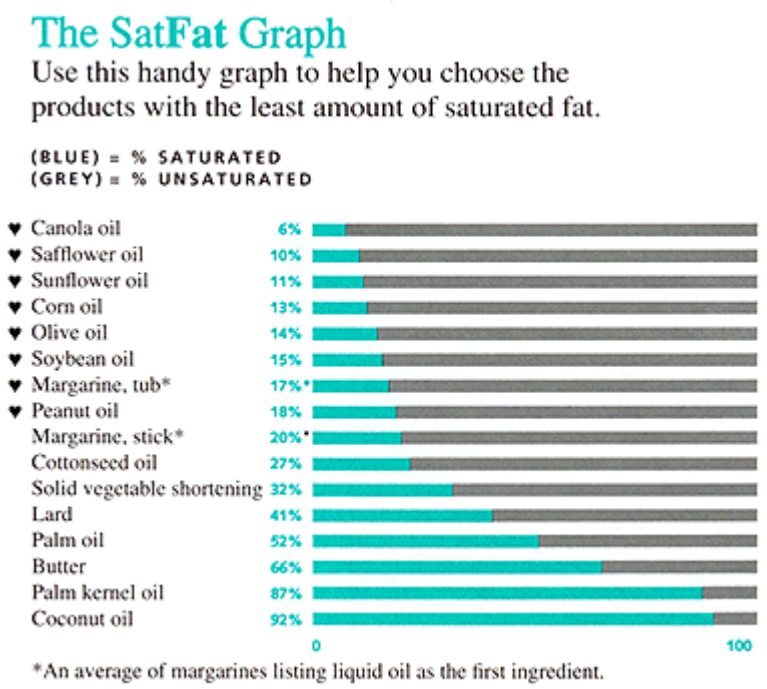
[18] http://www.cfsan.fda.gov/~dms/qhc-sum.html#olive

claim with a heart to indicate their beneficial fatty acid profile. Table 6 does not include an exhaustive list of potentially eligible vegetable oils. Any vegetable oil that meets or exceeds the unsaturated to saturated fat ratio (4:1) would be eligible. To prevent consumer confusion, ingredient statements for eligible oils, spreads, shortenings and foods would not be permitted to use "and/or" labeling for the primary oil source, unless all oils are eligible and similarly, blended oils would not be permitted unless they are comprised only of eligible oils. Finally, eligible oil(s) would appear before any non-eligible fat source in the ingredient statement of an eligible food.

TABLE 6: Fatty Acid Profile* of Oils Eligible to Bear Claim

Vegetable Oil	SFA	MUFA	PUFA	Unsat:sat ratio
Safflower	6.2	14.4	74.6	14.4
High-oleic Safflower	6.2	74.6	14.4	14.4
Canola	7.1	58.9	29.6	12.5
Mid-oleic Sunflower	9.0	57.3	29.0	9.6
Sunflower	10.3	19.5	65.7	8.3
Corn	12.9	27.6	54.7	6.4
Olive	13.8	73.0	10.5	6.0
Sesame	14.2	39.7	41.7	5.7
Soybean	14.4	23.3	57.9	5.6
Peanut	16.9	46.2	32.0	4.6
*Based on USDA Nutrient Database SR 19				

Figure 1



Source: http://www.nhlbisupport.com/chd1/Tipsheets/tipsheet-satfat.htm

Oil-containing foods (eligibility criteria summarized in Table 7):

The proposed claims would be restricted to oil-containing foods in the following categories: crackers, salads (including cabbage salad and other coleslaw-type products), salad dressings (including mayonnaise and mayonnaise-type dressings), sauces and dips (including tarter sauce) and grain, vegetable and fruit-based snacks including but not limited to chips and crisps that meet the following criteria:

1. The primary oil source (appears before all other non-eligible fat sources in the ingredient statement) in a food would be only eligible vegetable oils with an unsaturated to saturated fat ratio equal to or greater than 4:1.
2. Blends of oil would be permissible as long as only eligible oils are utilized.
3. Food ingredient statements could not include “and/or” labeling for primary fat sources unless all options are eligible vegetable oils.
4. Foods would be required to contain at least 4.5 grams of unsaturated fatty acids per RACC [19];
5. Foods that exceed the disqualifying levels for total fat, as defined by 21 CFR §101.14(a)(4), would be required to include the disclosure statement required by 21 CFR §101.13(h).
6. Saturated fat content of foods would not exceed 20 percent of the total fat content per RACC and the saturated fat disqualifier levels would apply. A disclosure statement such as: “See back panel for saturated fat information”

[19] Minimum unsaturated fat content must be based on analytical values, not labeled or rounded values.

would be required for foods that do not meet the definition of "low saturated fat" as specified in the Olive Oil QHC.

7. Foods would contain 0.5 grams or less of trans fat per RACC according to accepted rounding rules.
8. Foods would meet the definition for "low cholesterol"[20] (21 CFR §101.62(d)).
9. Foods would not exceed disqualifying levels for sodium per 21 CFR §101.14 (a)(4)).

TABLE 7. Nature of Foods Eligible to Bear the Claim	
Nutrient	Requirements
VEGETABLE OILS	
Unsaturated:Saturated Fat Ratio for Oil – Only these oils may be used in food products.	Must be liquid vegetable oil with U:S ≥ 4:1 (e.g.,corn, canola, sunflower, soybean, olive, safflower, sesame, peanut)
VEGETABLE OILS, SPREADS, SHORTENINGS AND OIL-CONTAINING FOODS	
Minimum Total Unsaturated Fat Content	4.5 g of total unsaturated fats per RACC
Saturated Fat Content	Not more than 20% of total fat content
Saturated Fat Disqualifier Level	<4g per RACC*
Total Fat Content	Disclosure per 101.13(h) Not applicable to oils, spreads and shortenings
Trans Fat Content	0 g per RACC‡
Cholesterol Content	Low Cholesterol
Sodium Content	≤ 480 mg*
‡ < 0.5 g per RACC * For small RACCs (30 g or less or 2 tbsp or less) per 50 grams; oils, spreads and shortenings are exempt from the 50 gram criterion	

The product categories eligible for the proposed claims were identified by an analysis of all foods consumed by 13,431 adult (≥20 years) participants of the 1999-2004 National Health And Nutrition Examination Survey (NHANES) who provided reliable 24-hour dietary recall data. Food categories were deemed eligible if they

[20] Per the definition of "low cholesterol", saturated fat must not exceed 2 g per RACC for foods and per 100 grams for main dishes and meals.

contained a variety of products that met the above claim eligibility criteria. Products eligible to bear the proposed claims based on these data are presented in **Table 8**. A list of all products in these categories (including those which would require reformulation to bear the proposed claims) is presented in Appendix I. Food manufacturers have already reformulated many products with healthier oils due to mandatory trans fat labeling and to meet the needs of more health-conscious consumers. Therefore, the data from NHANES reported herein is not a completely accurate reflection the current food supply.

Table 8. Foods Consumed by 1999-2004 NHANES Participants that Qualify for the Proposed Claims

Food Description	Frequency of consumption
Crackers	470
Crackers, NS as to sweet or nonsweet	51
Cracker, snack, low sodium	15
Cracker, snack	390
Crackers, cylindrical, peanut-butter filled	5
Crackers, sandwich-type, NFS	9
Salads, meatless	389
Apple salad with dressing	4
Apple and cabbage salad with dressing	1
Caesar salad (with romaine)	4
Carrots, raw, salad	17
Carrots, raw, salad with apples	2
Tomato and cucumber salad made with tomato, cucumber, oil, and vinegar	14
Cabbage salad or coleslaw, with dressing	313
Cabbage salad or coleslaw with apples and/or raisins, with dressing	10
Cabbage salad or coleslaw with pineapple, with dressing	2
Cucumber salad made with cucumber, oil, and vinegar	10
Artichoke salad in oil	6
Pea salad	6
Salad dressing, mayonnaise & mayonnaise-type dressing	309
Bacon dressing (hot)	5
Coleslaw dressing	4
French dressing	143
Fruit dressing, made with honey, oil, and water	1
Mayonnaise, imitation, cholesterol free	1
Russian dressing	15
Green Goddess dressing	1

Poppy seed dressing	17
Celery seed dressing	1
Thousand Island dressing	121
Sauces and dips	172
Clam sauce, white	2
Brown nut gravy, meatless	2
Sesame sauce	3
Spaghetti sauce, meatless, low sodium	2
Tartar sauce	163
Grain, Vegetable and Fruit Based Snacks	1,093
Salty snacks, corn or cornmeal base, corn chips, corn-cheese chips	278
Salty snacks, corn or cornmeal base, tortilla chips	762
Salty snacks, corn or cornmeal base, corn chips, corn-cheese chips, unsalted	8
Salty snacks, corn or cornmeal base, tortilla chips, unsalted	2
Salty snack mixture, mostly corn or cornmeal based, with pretzels, without nuts	14
Salty snacks, multigrain, chips	29

A. TOTAL FAT CONTENT RESTRICTIONS

Frito-Lay intends to apply the criteria for total fat restrictions specified by FDA in its letters of enforcement discretion for the Olive and Canola oil QHCs to the new claims. Specifically, FDA did not impose a low fat restriction for foods eligible to bear such claims, and elected not to apply the total fat disqualifier level to the pure oils or any foods containing them.

The criteria established for the proposed health claims do not restrict the total fat content of foods eligible to bear them. Because a minimum amount of unsaturated fat must necessarily replace saturated and trans fats, the claims cannot apply to low-fat foods. Notably, FDA has stated in accordance with the Dietary Guidelines that consuming diets low in saturated fat and cholesterol is more important in reducing the risk of CHD than consuming diets low in total fat.

The proposed health claims are particularly well-suited to oil-containing foods where the consumer may not yet be aware of or looking for foods made with the healthiest

vegetable oils. In fact, research indicates that consumers do not know what foods contain unsaturated fats or recommended vegetable oils (IFIC Food and Health Survey, 2006). In keeping with the spirit of the FDA's Task Force Final Report on Consumer Health Information for Better Nutrition (July 10, 2003) it would follow that better-informed consumers would choose foods containing vegetable oils with the lowest concentrations of saturated and trans fats and the highest amounts of MUFA and PUFA, which will ultimately improve their overall diets.

As provided in Section 403r(3)(A)(ii) of the FD&C Act, the Secretary may permit foods that exceed disqualifying levels for a given nutrient to bear the health claim if such claim is found to assist consumers in maintaining healthy dietary practices. As it is not the intent of the proposed health claims to promote increased intake of total fat, but rather to help consumers choose fats more wisely for better overall health, this exemption is appropriate. Exemption from the total fat disqualifier levels has been applied to health claims for plant sterol/stanol esters[21], nuts[22], walnuts[23], canola[24] and olive oils[25], and soy protein[26] (whole soybean) and coronary heart disease. In these cases it was determined that applying the disqualifying levels of total fat would "… unduly limit the foods that could contribute to beneficial effects from bearing the health claim" and that "foods labeled with the health claims would assist consumers in maintaining healthy dietary practices." The same rationale

[21] 21 CFR §101.83
[22] http://www.cfsan.fda.gov/~dms/qhcnuts2.html
[23] http://www.cfsan.fda.gov/~dms/qhcnuts3.html
[24] http://www.cfsan.fda.gov/~dms/qhccanol.html
[25] http://www.cfsan.fda.gov/~dms/qhcolive.html
[26] 21 CFR §101.82

would apply because the present proposed health claims would assist consumers in differentiating types of fat and understanding that all vegetable oils and oil-containing foods with the prescribed amount of unsaturated fats should replace saturated and trans fats in the diet while not increasing total daily calories. Moreover, the additional criteria to prohibit "and/or" labeling with ineligible fats or oils will help prevent consumer confusion. Therefore this notification stipulates that when foods exceed disqualifying levels for total fat per RACC, disclosure statements for total fat appear in immediate proximity to the health claims pursuant to 21 CFR §101.13(h).

B. CHOLESTEROL CONTENT RESTRICTIONS

Vegetable oils are naturally cholesterol-free and the definition of "low cholesterol" would not unduly limit the use of the health claim. Therefore vegetable oils, spreads, shortenings and oil-containing foods would be required to meet the FDA definition of low-cholesterol (21 CFR §101.62(d)). Oil-containing foods can be formulated to meet this requirement. This criterion is in accordance with those set forth in the Olive and Canola Oil QHCs.

C. SATURATED AND TRANS FAT CONTENT RESTRICTIONS

As with total fat content, the agency has granted exemptions to the general health claim criteria with regards to saturated fat. All vegetable oils are a mix of saturated, monounsaturated, and polyunsaturated fat. With the exception of canola oil, none of these oils would be able to achieve the FDA definition of low saturated fat and still meet the minimum effective amount of unsaturated fats required for the proposed

claims. FDA acknowledged this fact in their approval of the Olive Oil QHC. Therefore, in accordance with the rationale presented in the FDA response letter to this claim, all essentially pure vegetable oils, spreads and shortenings in the present proposed health claims would be subject to disqualifying limits for saturated fat (21 CFR §101.14) of no more than 4 grams per RACC (14g) but would be exempt from the 50 gram criterion for products with small serving sizes. Frito-Lay believes the saturated fat disqualifier value (including the 50 gram criterion) should also apply to foods containing oils that qualify for the claim. However, a requirement that such foods meet the definition of low in saturated fat (21 CFR § 101.62 (c)(2)) would be overly restrictive and is not necessary to ensure appropriate use of the claim as stated by FDA in its response to the Olive Oil QHC.

The proposed eligibility criteria would require that oil-containing foods (some of which may contain small amounts of fats or oils other than those that qualify for the claim) would be required to maintain an unsaturated to saturated fat ratio of 4:1 (or no more than 20 percent of total fat as saturated fat). This requirement would ensure that the saturated fat content of oil-containing foods would be kept well below disqualifying levels (21 CFR §101.14(a)(4)) for this dietary constituent. This criterion would ensure that saturated fat content stays as low as possible but still allows for small additions of other fat sources such as, non-eligible oils, cheese or fat-based coatings or sauces. As a result, the total unsaturated fat content of such foods would essentially overwhelm their saturated fat content regardless of the level of total fat. As well, the allowable saturated fat content of such foods would decrease

in parallel with their total fat content. For example, a food with 10 grams of fat would be limited to 2 grams of saturated fat, whereas a food with 8 grams of total fat would be limited to no more than 1.6 grams of saturated fat per RACC. Additionally, in accordance with the FDA's response to the Olive Oil QHC, any vegetable oil, spread, shortening or oil-containing food that does not meet the requirement for "low saturated fat" (21 CFR § 101.62 (c)(2)) would be required to bear a disclosure statement such as: "See back panel for saturated fat content." A more detailed discussion of the saturated fat content of foods eligible to bear the health claims is presented in later sections of this document.

The present notification would require that vegetable oils, spreads, shortenings and oil-containing foods contain no more than 0.5 grams of trans fat per RACC in accordance with the FDA regulation on trans fat labeling (21 CFR §101.9(c)(2)(ii)) which recognized the cholesterol-raising effect of trans fats. This requirement would ensure that all products bearing the claim would have a trans fat declaration of zero grams per serving.

D. THE 10% DV MINIMUM NUTRIENT CONTENT REQUIREMENT

Frito-Lay strongly believes that application of the 10% DV minimum nutrient content requirement (21 CFR §101.14(e)(6)) to the proposed claims would be unnecessary and inappropriate. It is clear that many foods low in or devoid of the six nutrients (vitamins C, A, calcium, iron, protein, or fiber) required under this provision make important contributions to a healthy diet. In addition, analysis of the 1999-2004

NHANES database presented in **Table 9** shows that intake of the positive nutrients protein, carbohydrate, total dietary fiber, calcium, phosphorus, magnesium, copper, potassium and vitamin E was *higher* ($p<0.01$) among women who consumed at least one product that qualifies for the proposed claims than among those who did not. Analogous data for adult men showed higher intakes of these nutrients as well as thiamin, riboflavin, vitamin B-6, folate, iron and zinc in consumers vs. nonconsumers of products that qualify for the proposed claims. The food categories included in this analysis were crackers, salads, salad dressings, sauces and dips as well as grain, vegetable and fruit-based snacks.

Table 9. Mean Nutrient Intake (EAR/AI) of Participants in the 1999-2004 NHANES Who Consumed at Least One Food that Meets Criteria for the Proposed Claim Among Five Categories[1] Compared to Participants Who Did Not Consume Such Foods[2]

Nutrient	Women 20+ years		Men 20+ years	
	Consumers (n=1,178)	Nonconsumers (n=5,889)	Consumers (n=951)	Nonconsumers (n=5,413)
Protein	184.6*	174.6	223.8*	211.4
Carbohydrate	241.5*	226.9	348.3*	309.6
Total Dietary Fiber	64.1*	58.2	57.5*	49.3
Vitamin A (RAE)	117.5	112.0	110.5	105.8
Alpha Tocopherol (mg)	59.9*	50.2	76.6*	64.5
Vitamin C	146.2	140.0	144.0	132.3
Thiamin	155.1	152.6	202.6*	188.8
Riboflavin	205.2	199.1	240.5*	223.6
Niacin	177.2	174.7	241.1	233.4
Vitamin B-6	135.7	130.7	201.2*	183.6
Folate (DFE)	146.8	145.5	208.1*	191.8
Vitamin B-12	222.9	204.8	332.6	315.2
Calcium	76.8*	69.7	106.1*	90.5
Phosphorus	208.0*	190.7	292.1*	264.0
Magnesium	99.2*	90.2	105.5*	93.3
Iron	202.4	196.6	319.8*	298.1
Zinc	149.0	142.1	161.3*	150.1
Copper	166.7*	155.0	239.8*	215.1
Sodium	230.5*	201.7	313.2*	280.5
Potassium	53.4*	49.9	71.3*	66.4
Selenium	207.6	200.9	296.3	286.8
Vitamin K	119.2*	96.4	92.7*	72.7

[1] Crackers, salads, salad dressings, sauces and dips and grain, vegetable and fruit based snacks.
[2] Mean is sample-weighted
*p<0.01 for difference between consumers and nonconsumers estimated by the linearization method of SUDAAN.

These data show that nutrient intake is not compromised among individuals who consumed products that qualify for the proposed claims and clearly demonstrate that the 10% DV minimum nutrient content requirement is unnecessary.

As discussed in more detail later in this notification, the agency has waived or modified this criterion in multiple health claims including: Plant sterol and stanol esters and coronary heart disease[27], nuts and coronary heart disease[28], walnuts and coronary heart disease[29] and whole grains and coronary heart disease[30]. The rationale for this position was based on the findings that such health claims would assist consumers in maintaining healthy dietary practices that are consistent with the Dietary Guidelines for Americans. Frito-Lay believes this rationale also applies to the proposed health claims because they are specific to replacing unhealthy fats with healthy fats and would not increase total fat or calorie consumption as specified in the claim language.

E. ADDITIONAL CONSIDERATIONS

[27] 21 CFR §101.83
[28] http://www.cfsan.fda.gov/~dms/qhcnuts2.html
[29] http://www.cfsan.fda.gov/~dms/qhcnuts3.html
[30] http://www.cfsan.fda.gov/~dms/flgrain2.html

The FDA Task Force Final Report on Consumer Health Information for Better Nutrition Initiative (2003)[31] established the agency's position on health related messaging.

> *FDA "seeks to help consumers improve their understanding of how their dietary choices may influence their health, to promote competition among product developers to find better ways to help improve health through better diets, and ultimately to prevent serious and life-threatening diseases through better dietary choices by Americans." (Overview paragraph 1)*

As described, the proposed health claims would arm the consumer with better information about foods, and in particular how to choose healthier fats and thus enable and encourage wise dietary choices that benefit long-term health. Unduly limiting foods to bear a health claim that would promote healthier dietary practices is not is accordance with the FDA initiative.

Data from the 1999-2004 NHANES show that the proposed claims would not contribute to the incidence of overweight or obesity. The data presented in **Table 10** show that there was no difference in BMI among consumers and non-consumers of the proposed eligible foods despite the fact that the mean energy intake of participants who consumed products in any of the five categories included in Table 8 that meet the criteria for the proposed claims was higher than those who did not for women (2,018 vs. 1,812 kcal; $p<0.01$) and for men (2,906 vs. 2,571 kcal; $p<0.01$).

Table 10. Mean Body Mass Index of Participants in the 1999-2004 NHANES Who Consumed at Least One Food that Meets Criteria for the Proposed Claim

[31] http://www.cfsan.fda.gov/~dms/nuttftoc.html

Among Five Categories Compared to Participants Who Did Not Consume such Foods

Food Group	Sample size (n)	BMI (kg/m^2)[1]
All adults (20+ years)	13,062	28.1 ± 0.1
Any of the five food groups		
▪ Consumers	8,006	28.1 ± 0.1
▪ Nonconsumers	5,056	28.1 ± 0.1
Crackers		
▪ Consumers	1,695	27.9 ± 0.2
▪ Nonconsumers	11,367	28.1 ± 0.1
Salads, meatless		
▪ Consumers	951	29.1 ± 0.3*
▪ Nonconsumers	12,111	28.0 ± 0.1
Salad dressings and mayonnaise		
▪ Consumers	3.932	28.1 ± 0.2
▪ Nonconsumers	9.130	28.1 ± 0.1
Sauces and dips		
▪ Consumers	2,417	28.0 ± 0.2
▪ Nonconsumers	10,645	28.1 ± 0.1
Grain, Vegetable and Fruit Based Snacks		
▪ Consumers	2,662	28.1 ± 0.2
▪ Nonconsumers	10,400	28.1 ± 0.1

[1] Mean ± SEM; Mean is sample-weighted and standard error estimated by the linearization method of SUDAAN.
*$p<0.01$ for difference between consumers and nonconsumers

Frito-Lay believes the data in Table 9 provide considerable reassurance that use of the proposed claims will not contribute to overweight or obesity despite the apparent discrepancy in energy intake noted above. BMI was measured directly on the NHANES subjects and is an objective measure of overweight and obesity. This measure is less prone to error than the assessment of energy intake using 24-hour recall questionnaires which are known to be subject to considerable error.

More importantly, however, the proposed claim language specifically states, "***To achieve this benefit, total daily calories should not increase."*** This language reflects the intent of the claim which is to help consumers identify foods made with healthy fats, and to provide an incentive for food manufacturers to develop and market such products (see below).

The proposed health claims would also promote competition among food manufacturers to develop and market products that will ultimately improve the overall diet. For example, food manufacturers are working diligently to remove trans fat-containing oils from their products in response to scientific evidence and mandatory labeling. The proposed health claims would provide great incentive for food manufacturers to replace unhealthy fats in their products with healthy vegetable oils, thereby improving the overall nutritional quality of the food supply. Without such incentive, food manufacturers may choose to replace unhealthy oils containing trans fats from partially hydrogenated oils with fat sources high in saturated fat, such as tropical oils or with animal fats. In the trans fat labeling regulations, the FDA stated that it does not view replacement of trans fats with saturated fats as an appropriate substitution (68 FR 41434 at 41481).

The final regulation on health claims (58 FR, 2478, January 6, 1993), made several things clear. First, no individual food would be prohibited *per se* from bearing a health claim based on its categorization (58 FR, 2478 at 2521). Second, foods that bear health claims should be consistent with the current dietary guidelines (58 FR, 2478 at 2521). Third, a claim should enable the public to comprehend the information and understand the relative significance of that information in the context of the total diet (58 FR, 2478 at 2521). Fourth, the FDA must consider the role that a particular food plays in the total diet, and the effect that its nutrient levels will have on a person's ability to structure a healthy diet (58 FR, 2478 at 2521). Fifth, health

claims should be limited to foods that contribute nutrients and not just calories (58 FR, 2478 at 2521).

Frito-lay believes that the proposed health claims and criteria fully encompass health claim expectations as stated in the regulations noted above. The proposed health claims would permit all eligible foods to bear the claim. The proposed health claims are consistent with the current Dietary Guidelines for Americans regarding dietary fat intake. The regulations for health claims in 21 CFR §101.9(k)(1), 101.14(c)-(d), & 101.70 were promulgated when the Dietary Guidelines for Americans recommended "low fat" diets, which is no longer the case. FDA concurs that the type of dietary fat is more important than total fat consumed as part of a calorie-controlled diet. The claims as proposed would help the consumer understand the health benefit is achieved when vegetable oils are *substituted* for solid fats.

The 2005 Dietary Guidelines for Americans specifically state that most fats consumed should be MUFA and PUFA-predominant fats from foods such as fish, nuts, or vegetable oils. The Guidelines specifically state that, in addition to keeping saturated and trans fat intakes as low as possible, individuals should also "choose products low in such fats and oils." This position is the very essence of the proposed claims -- to provide consumers with science-based information so that they may identify *foods* that contain healthy oils and low amounts of saturated and trans fats as well as the more obvious cooking oils, spreads, and dressings. The replacement of unhealthy fats with vegetables oils is the direct health benefit of the proposed health claims. Such claims would promote healthier dietary choices and therefore

do not require the 10% minimum nutrient content requirement. This position is supported by the authoritative statements herein and the regulations on trans fat labeling (68 FR, 41434). As noted previously, the calculated reductions in CHD risk presented in those regulations were based on replacing trans fats with unsaturated fats and no other considerations were made beyond isocaloric fatty acid substitution. In the context of the total diet, the proposed health claims will promote greater unsaturated fat intakes with concurrently lower saturated and trans fat intakes, and total calories will not increase to achieve the heart healthy benefits.

Furthermore, the nutritional value of vegetable oil goes beyond the substitution effect (replacing saturated and trans fats with unsaturated fats), because eligible oils under the proposed health claims would provide essential fatty acids which are required for optimal health (**Table 11**). Vitamin E has been identified as a "nutrient of concern" by the 2005 Dietary Guidelines for Americans and vegetable oils are an important source of vitamin E in the diet (**Table 12**). Vegetable oils also contain free and esterified phytosterols (**Table 13**). Plant sterols and stanols are hypocholesterolemic because they interfere with the absorption of cholesterol and can reduce LDL-C by up to 15 percent (Grundy, 2005). Optimal hypocholesterolemic effects are observed at intakes of approximately 2g/d, however lower intakes also produce beneficial reductions in LDL-C (Katan et.al., 2003). The NCEP (2002) and the American Heart Association Diet and Lifestyle Recommendations (Lichtenstein et al, 2006) acknowledge the potential value of phytosterols in the management of CHD. All oils eligible for the proposed health claim will contribute to the total intake of these substances. Finally, dietary fats are essential for the absorption of fat-soluble

vitamins (A, D, E, K). Though vegetable oils do not contain one of the six nutrients required under 21 CFR §101.14(e)(6), they are not devoid of nutritional value which is why the 2005 Dietary Guidelines does not consider vegetable oils discretionary calories in contrast to the saturated and trans fats in tropical oils and animal fats. The FDA clearly states that the definition of "nutritive value" is not limited to only six predetermined nutrients, but that it is flexible to account for substances that can play a major role in reducing the risk of certain chronic diseases (58 FR, 2478 at 2488).

Table 11. Essential Fatty Acid Content of Proposed Eligible Vegetable Oils
Based on values from USDA Nutrient Database (SR 19)

Oil	n-6 in 1 Tbsp (g)	AI n-6 (men) (%)	AI n-6 (women) (%)	n-3 in 1 Tbsp (g)	AI n-3 (men) (%)	AI n-3 (women) (%)
Canola	2.8	16.5	23.3	1.3	81.3	118.2
Safflower	10.2	60.0	85.0	0	0.0	0.0
Sunflower	8.9	52.5	74.4	0	0.0	0.0
Mid-Oleic Sunflower	3.9	23.1	32.8	0	0.3	0.5
Soybean	6.9	40.8	57.8	0.9	57.8	84.1
Corn	7.3	42.8	60.7	0.2	9.9	14.4
Olive	1.3	7.8	11.0	0.1	6.4	9.4
Sesame	5.6	33.0	46.8	0.04	2.6	3.7
Peanut	4.3	25.4	36.0	0	0.0	0.0

AI of n-6: 17 g/d men, 12 g/d women
AI of n-3: 1.6 g/d men, 1.1 g/d women

TABLE 12 Vitamin E Content of Healthy Oils
Based on values from USDA Nutrient Database (SR 19)

Vegetable Oil	Vitamin E (mg/Tbsp[14 g])*	% Daily Value
Safflower	4.6	23

Canola	2.4	12
Mid-oleic Sunflower	5.6	28
Sunflower	5.6	28
Corn	1.9	9.5
Olive	1.9	9.5
Soybean	1.3	6.5
Peanut	2.1	10
* 1 mg = 1.49 IU RDI for vitamin E is 30 IU		

Table 13. Total Free and Esterified Sterol Content of Selected Vegetable Oils

Oil Sample	Sitosterol (mean)	Campesterol (mean)	Stigmasterol (mean)	Brassicasterol (mean)	Avenasterol (mean)	Sitostanol (mean)	Campestanol (mean)	Total Sterol Content
Canola	377	208	142	46.7	22.4	2.7	1.7	800.5
Corn	1,348	263	121	nd	339	30	19	2,120
Soybean	141	45.5	49.1	0.2	5.8	4.2	2.2	248
Safflower	120.7	28	14.8	nd	18.3	9.6	2.6	194
Peanut	115	23.7	12	1.2	12.9	2.5	0.9	168.2
Sesame	333	75.5	35	nd	52.5	1.9	1.4	499
Olive	126	4.3	2.5	nd	16.7	3.1	0.7	153.3
Sunflower	194	27.1	17.7	2.1	18.7	2.9	1.2	263.7

Source: Phillips et al, J Food Comp Analysis, 2002.

In conclusion, the proposed health claims will arm consumers with information to make healthy choices regarding dietary fats. First, the claims will apply only to foods that will contribute unsaturated fats and keep saturated and trans fats as low as possible in keeping with the current Dietary Guidelines for Americans. Second, the claims will help to increase consumer awareness and knowledge of MUFA and PUFA, to help individuals identify healthy vegetable oils and to understand that substituting these fats for saturated and trans fats will contribute to a heart healthy diet. Finally, the health claims will provide incentives to food manufacturers to use

healthy oils in their products as they work to reformulate high trans fat or saturated fat-containing foods. The overall effect of the claims will be a better informed consumer and a healthier food supply.

X. BENEFIT TO THE CONSUMER

Awareness and knowledge of healthy foods are key for the consumer to maintain healthy dietary practices. Health claims, including the proposed health claims for unsaturated fats and CHD, are important to this end. The FDA and The International Food Information Council (IFIC), a non-profit organization which disseminates science-based information on nutrition and food safety and consumer understanding of these issues, have conducted quantitative consumer research studies (FDA Health and Diet Survey, 2004; IFIC Food and Health Survey, 2006) on consumer awareness and perceptions of diet and health outcomes.

In brief, the IFIC Foundation Food and Health Survey explored two key issues: (1) how American consumers think and feel about health, diet (including overall diet and principal nutrients such as fats, sugars, and carbohydrates), physical activity, and weight, and (2) how American consumers' knowledge and attitudes impact behavior and use of health information and tools when making food choices. The survey contained numerous questions specific to dietary fatty acids.

The Survey found that about two-thirds of consumers are "concerned" about the type and amount of fat they consume. While the majority of those questioned indicated they had heard of most types of fats, awareness of saturated fats was significantly

higher than that for MUFA and PUFA. Animal fats, partially hydrogenated oils, saturated fats, and trans fats were more likely to be rated as “unhealthful.” Perhaps most telling was the finding that 30-50 percent of respondents perceived most fats to be “neither healthful nor unhealthful” and that four in ten consumers aware of unsaturated fats perceived them to be “unhealthful”. Consumption trend results indicated that most consumers have not changed their eating behavior with regard to fats.

Results of the FDA survey were very similar to the IFIC survey. This survey specifically tested consumer awareness of fats and their knowledge of the relationships between different types of fat and CHD risk. While the majority of consumers were aware of MUFA and PUFA (77 and 62 percent, respectively), they reported that they did not know what effects these fatty acids have on CHD risk or believed PUFA and MUFA have no effect on risk (64 percent PUFA; 68 percent MUFA). Moreover, 21 percent believed that PUFA increase the risk for CHD and 16 percent believed MUFA raise CHD risk. Only 12 percent who had heard of PUFA correctly identified its relationship with CHD risk and only 10 percent did so for MUFA. Seventy-five percent of consumers who had heard of saturated and 32 percent who had heard of trans fats correctly identified their relationships with CHD risk.

Collectively, these surveys show that consumers have a better awareness and understanding of saturated fats and trans fats compared to unsaturated fats but that

they remain confused about fats and oils and have therefore not changed their consumption behaviors.

The 2005 Dietary Guidelines for Americans state that most fats should come from mono and polyunsaturated sources, yet the Diet and Health Survey (FDA) and Food and Health Survey (IFIC) found that the majority of consumers aware of both type of fats do not understand their relationship to CHD risk and are not trying to increase their consumption. Moreover, the majority of consumers aware of unsaturated fats say they don't know what foods contain them. The proposed health claims for unsaturated fats and coronary heart disease would serve to increase the consumer's understanding of the different types of fats as well as serve to help them identify the types of oils in the foods they commonly consume. In doing so, the proposed health claims will help the consumer maintain healthy dietary practices.

XI. REVIEW OF SCIENTIFIC LITERATURE: UNSATURATED FATS AND CHD

The scientific evidence in support of the proposed health claims has been thoroughly reviewed and summarized within the authoritative statements that support these claims. These documents provide balanced representations of the literature which consistently demonstrates that replacing saturated and trans fats with MUFA and PUFA reduces the risk of CHD as part of an overall healthy diet. The authoritative documents and bibliographies are available in **Appendices A – G**. To provide further support for these authoritative statements we have summarized the studies used to determine the minimum effective amount of unsaturated fats for the

proposed health claims (see Table 4) and studies published after the authoritative statements (after 2002).

A. RESEARCH TO SUPPORT THE PROPOSED MINIMUM DAILY EFFECTIVE DOSE OF UNSATURATED FATS

Mata et.al. (1992) investigated the effects on plasma lipoproteins of diets rich in saturated fat or unsaturated fats from olive oil (and sunflower oil which was not considered for the minimum effective unsaturated fat dose). Following a four week run-in period during which time energy requirements were assessed by 24-hr recall and a food frequency questionnaire, 21 healthy, normolipidemic women (teachers living in a boarding school where all meals were prepared) first received a moderately high fat diet (35%) rich in saturated fat (SFA 19%, MUFA 14%) for four weeks, followed by a diet rich in MUFA (SFA 11%, MUFA 22%) for six weeks, in two consecutive phases. Only the type of oil used in the preparation of the meals differed between the test diets. Intakes of cholesterol, fiber, carbohydrate, PUFA, and protein were held constant between the dietary interventions. Plasma TC decreased by 8.9% (5.27mmol/L to 4.80 mmol/L) in subjects after consumption of the high-MUFA diet, compared with the high-SFA diet. This change was accounted for largely by an 18.6% (3.44mmol/L to 2.80mmol/L) decrease in LDL-C. Both HDL-C and TG concentrations increased significantly during the MUFA phase of the trial. Plasma HDL-C increased by 5.6% (1.42mmol/L to 1.50mmol/L), and TG increased by 10.5% (0.95mmol/L to 1.05mmol/L). The increase in TG was attributed to elevations in five women with the highest body weight. The authors conclude that in

this female population a diet rich in MUFA produced a lipoprotein profile consistent with decreased atherogenic risk. The difference in total unsaturated fats between the olive oil based diet and the high-saturated fat diet was 17.8 grams per 2000 calories. This study was included in the FDA determination for the minimum effective dose of MUFA in the Olive Oil QHC.

A study by Lichtenstein et al (1999) compared six diets with differing trans fat content against liquid soybean oil and butter to determine the cholesterolemic effects. Thirty-six men and women with moderately elevated LDL-C (>130 mg/dl) consumed six diets in random order for 35 days each. The subjects and investigators were blinded to the test treatments. All foods were provided to the subjects and they consumed one meal on site four times per week. Each diet provided 30% of total calories as fat in which two-thirds was provided by liquid soybean oil (SO), semiliquid margarine (LM), soft margarine (M), shortening (S), or stick margarine (SM). Trans fat content of each diet was 0.55, 0.91, 3.30, 4.15, and 6.72% of total energy for the SO, LM, M, S and SM diets, respectively. The saturated fat content of the butter-based diet was twice that of the other test diets at 16.7% of energy. MUFA content was consistent between all diets, but PUFA content was higher on the SO and margarine based diets compared to the butter based diet. Compared to the butter diet, total and LDL- C were significantly reduced on the SO, margarines and S diets. The lowest total and LDL-C levels were achieved on the SO and LM diets and cholesterol levels increased progressively with increasing saturated and trans fat content. LDL-C was reduced by 12 and 11%

on the SO and LM diets, respectively. HDL-C levels were significantly reduced on the SM (-6%, $p<0.05$ vs. butter) diet. The total to HDL-C ratio was lowest after the SO and LM diets and highest on the SM diet ($p<0.05$ vs. soybean, semi liquid and soft margarines). The ratio was not significantly different between butter and stick margarine diets. The difference in total unsaturated fats between the soybean oil based diet and the butter diet was 22.5 grams per 2000 calories. Because the authoritative statements do not include reference to trans fats, trans fat data were not considered for the minimum effective unsaturated fat dose, however this study shows that replacement of diets high saturated fat or trans fats (difference in total unsaturated fat was 13 g per 2000 calories) with soybean oil which is high in PUFA elicits comparable reductions in TC and LDL-C ($P < 0.05$).

Kris-Etherton *et.al.* (1999) compared the lipid and lipoprotein profiles of 22 healthy men and women after consumption of an Average American Diet (AAD) or three intervention diets high in MUFA for four weeks in a double-blinded, randomized, cross-over trial. MUFAs in the intervention diets were provided by olive oil (OO), peanut oil (PO), or peanuts and peanut butter (PPB). The investigators supplied all foods during the trial periods, and subjects were not allowed to consume non-study foods or beverages. Compliance was monitored by body weight measurements and a dietary assessment questionnaire administered daily. Subjects were allowed a four to 11 day break between study periods in order to enhance compliance. Fat intake was constant across study phases at 34 to 36% of energy. Dietary intakes of MUFA were higher during the MUFA intervention periods and accounted for 17% of

energy on the PO diet, 21% on the OO diet and only 11% during the AAD phase. Saturated fat content contributed 7% of energy on the OO and PO diets and 16% on the AAD diet. PUFA intakes were 6% of energy for the OO diet, 9% on the PO diet and 10% on the PPB diet. All three intervention diets resulted in similar, significantly lower serum TC, LDL-C, and TG compared to the AAD, without adversely affecting HDL-C levels. Compared to the AAD, subjects on the OO and PO diets had ≈10% lower TC (4.79 mmol/L OO, 4.93 mmol/L PO vs. 5.41 mmol/L AAD) and ≈14% lower LDL-C (2.98 mmol/L OO, 3.13 PO vs. 3.52 mmol/L AAD). Subjects on the PO diet had TG 13.5% lower than in subjects on the OO diet (1.15mmol/L vs. 1.33 mmol/L). HDL-C levels were almost identical in subjects on the OO diet compared to the AAD group (1.28 mmol/L vs. 1.29 mmol/L, respectively). This study also included a fifth dietary group based on the AHA Step II diet that was low in fat (25% of energy). Compared to this group, the OO and PO diet groups had a ≈ 21% lower TG (1.15 mmol/L OO, 1.18 mmol/L PO vs. 1.48 mmol/L AAD), but did not differ significantly in TC, LDL-C or HDL-C levels[32]. The authors concluded that "a high-MUFA, cholesterol-lowering diet is superior to the average American diet and a low-fat diet such as the Step II diet" especially since, unlike the Step II diet, the high-MUFA diet lowers TG and does not decrease HDL-C. Compared to the AAD diet, TC and LDL-C levels were significantly reduced with a difference in total unsaturated fats of 20 grams/2000 calories for the OO diet and 17.8 grams/2000 calories on the PO diet. Despite the higher saturated fat content of PO, the authors concluded that the higher PUFA content of PO may account for the higher TG concentrations on the OO diet.

[32] The superscript for the TC value of the Step II diet in Table 2 should be "b" rather than "a" as printed in the paper (personal communication with the senior author).

Vega-Lopez et al (2006) designed a trial to assess the effects of hydrogenation (trans fat) and degree of saturation on plasma lipids and lipoproteins. Fifteen generally healthy subjects (5 men, 10 postmenopausal women) with LDL-C greater than 130 mg/dl completed the study. Each diet phase was 35 days. All foods were provided to the subjects and the diets were designed to provide similar amounts of total fat (28-32% energy), carbohydrate, protein, fiber and cholesterol. The only difference between the diets was type of fat used. Two-thirds of the total fat was provided by partially hydrogenated soybean oil (PHSO), liquid soybean oil (SO), palm oil (PO) or canola oil (CO) which provided 20% of total calories. The fatty acid profiles (% energy) of the diets were as follows: PHSO contained 8.5% SFA, 4.15% trans fat, 10% MUFA, 8% PUFA, the PO diet contained 14.8% SFA, 11% MUFA, 3.5% PUFA, the SO diet contained 7.3% SFA, 8% MUFA, 12.5% PUFA, and the CO diet contained 6.4% SFA, 15% MUFA, and 8.7% PUFA. Total and LDL-C concentrations were significantly lower after the SO (220 mg/dl, 145 mg/dl) and CO (210 mg/dl, 140 mg/dl) diets vs. the PHSO (235 mg/dl, 162 mg/dl) and PO (240 mg/dl, 165 mg/dl) diets ($P < 0.05$). No differences were observed in TG or HDL-C concentrations between the diets. The authors concluded that equivalent amounts of palm oil or partially hydrogenated soybean oil produce similar and less favorable CHD risk profiles than oils high in unsaturated fats. They also recommended that palm oil should not be considered as an alternative to trans fat containing oils. Oils high in either MUFA or PUFA are preferred to reduce CHD risk biomarkers. The difference in total unsaturated fats between the PO and SO diets was 13.8

grams/2000 calories which produced an 8% and 12% lower concentrations of TC and LDL-C. The difference in unsaturated fats between the SO and PHSO was smaller and produced similar lipid responses.

Baudet et.al. (1988) examined the effect of diets that provided 15.6 percent of energy (% en) as low erucic acid rapeseed oil (equivalent to canola oil), milk fat, sunflower oil or peanut oil on serum lipids using a randomized, cross-over design with six-week intervention periods. The subjects were 20 healthy nuns living in a Benedictine monastery (mean age = 39 years) who had normal serum lipid values at baseline (TC = 208 mg/dl; LDL-C = 137 mg/dl; HDL = 69 mg/dl). The subjects had consumed the same diet for several years before the start of the study. The average energy content of all diets was 2,000 kcal/d and the macronutrient distribution was similar (total fat 30% en; CHO 54% en; protein 30% en). The cholesterol content of the high SFA diet was 400 mg/d compared to 300 mg/d for the other three diets. The fatty acid distribution (presented as % weight of total fatty acids of SFAs, MUFAs and PUFAs) for the high SFA diet was 70%, 27.8% and 2.2%, respectively. The fatty acid distribution for the peanut oil diet was 15% SFA, 42.5% MUFA, and 35.9% PUFA, 7.0% SFA, 58.4% MUFA, and 33.4% PUFA for the canola oil diet and 11% SFA, 17% MUFA and 71% PUFA for the sunflower diet. Serum TC and LDL-C concentrations were lowest after the canola and sunflower oil diets compared to the milk fat diets ($P<0.01$). TC and LDL-C responses were weaker on the peanut oil diet, but remained significantly lower compared to the milk fat diet. The canola oil diet resulted in lower ($p<0.01$) blood TC than the sunflower oil diet and in lower

(p<0.01) LDL-C than the sunflower and peanut oil diets. TG concentrations were lowest on the peanut (55 mg/dl) and sunflower (53 mg/dl) oils diets compared to the milk fat (72 mg/dl) diet (P<0.01). This study shows that peanut oil is effective, if to a slightly lesser extent than canola oil, in reducing lipid biomarkers of CHD risk when compared to a diet higher in SFA. The total unsaturated fat difference between the peanut oil diet and the milk fat diet was 16.2 grams/2000 calories. The difference between the canola and milk fat diets was higher at 21 grams/2000 calories, which may account for the greater reductions in TC and LDL-C on the canola oil diet. The experimental diets were very similar in macronutrient content, but cholesterol concentrations differed by 100 mg/d. The theoretical effect of differing cholesterol intakes, in this case 100 mg per day, would be very small (3.35 mg/dl for TC and 2.2 mg/dl for LDL-C) based on calculations using the Hegsted equation (Hegsted 1993). This calculation shows that the effect of the small difference in cholesterol content between the experimental diets on serum lipids is very small compared to that prompted by the differences in fatty acid intake. Therefore, the small effect of cholesterol does not compromise use of this study for the calculation of minimum effective dose of unsaturated fatty acids for the proposed claims.

Olive, soybean, and peanut oil studies were selected to determine the minimum effective dose of unsaturated fats because they have been clinically proven, under rigorous protocols where macronutrient intakes were constant and differed only in type of fat used, to reduce total and LDL-C when they replace SFA in the diet. As well, these oils have higher saturated fat contents than other oils that have been demonstrated to lower plasma lipids, such as corn, canola and sunflower oils.

Therefore by basing the calculations for the minimum daily dose of unsaturated fats (necessary to elicit clinically significant reductions in total and LDL-C) on olive, soybean, and peanut oils it will ensure that all oils eligible per the criteria proposed will favorably affect CHD risk. To base the calculation on oils with lower SFA content would generate a minimum unsaturated fat dose that may not apply to higher SFA oils.

B. RESEARCH PUBLISHED AFTER 2002

Mensink et al (AJCN 2003) conducted a meta-analysis that included 60 controlled trials to determine the effects of fatty acids on serum lipids and lipoproteins. In all trials fatty acids were exchanged with other fatty acids or carbohydrates. Only original research studies were considered and key criteria included: (1) highly controlled food intake with dietary fats as the sole variable; (2) constant intake of cholesterol between diet treatments; (3) parallel, cross-over or Latin-square designs that included control groups; (4) adequate feeding periods of 13 days or more to allow for serum lipids to reach new steady-state; (5) and only generally healthy adult subjects with no known disturbances in lipid metabolism. Mean intake values were 34.3%, 10.2%, 13.5% and 8.8% of energy from total fat, saturated fat, MUFA, and polyunsaturated fat.

Regression analyses showed that the total:HDL ratio was significantly reduced when unsaturated fats isoenergetically (1% en) replaced saturated fat and carbohydrate. The observed changes were in excellent agreement with predicted changes in the

ratio (R=0.99). The predicted changes in total:HDL, LDL-C and HDL are presented in **Figure 2.** Moreover, isoenergetic replacement of saturated fats with carbohydrates did not improve the total:HDL ratio. It was determined that all types of fat increase HDL and reduce TG relative to carbohydrate. As well, unsaturated fats, particularly PUFA, reduce apo B concentrations. **Figure 3** shows the predicted changes in total:HDL when different fat sources replace 10% of fat representative of the average American diet.

Figure 2

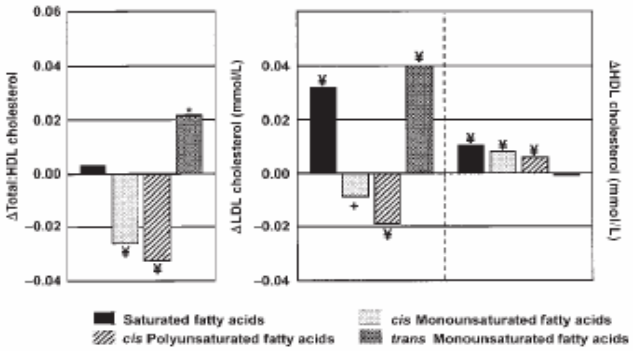


FIGURE 1. Predicted changes (Δ) in the ratio of serum total to HDL cholesterol and in LDL- and HDL-cholesterol concentrations when carbohydrates constituting 1% of energy are replaced isoenergetically with saturated, *cis* monounsaturated, *cis* polyunsaturated, or *trans* monounsaturated fatty acids. $^{*}P < 0.05$; $^{+}P < 0.01$; $^{¥}P < 0.001$.

Figure 3

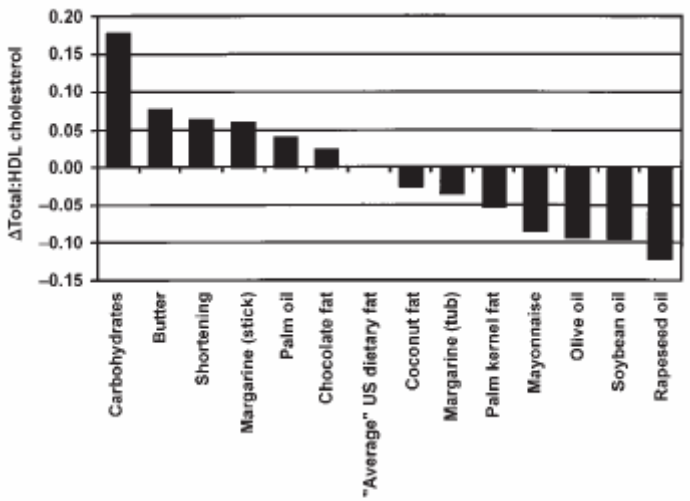


FIGURE 4. Predicted changes (Δ) in the ratio of serum total to HDL cholesterol when mixed fat constituting 10% of energy in the "average" US diet is replaced isoenergetically with a particular fat or with carbohydrates.

This meta-analysis provide strong evidence that substituting unsaturated fats for saturated fats as part of low and moderate fat diets significantly improves lipid biomarkers of CHD risk. Many of the studies included in this meta-analysis have been cited in the authoritative statements.

A study by Montoya et al (2002) compared the effects of moderate fat diets enriched in SFA, MUFA or PUFA on blood lipids in forty-one healthy volunteers (17 women, 24 men). All diets contained 35% energy as fat which were enriched with either palm (PO), olive (OO) or sunflower (SO) oils and provided equal amounts of protein (15%) carbohydrate (50%), cholesterol (<300 mg/d) and fiber (25 g/d). SFA, MUFA and PUFA content of the PO, OO, and SO diets were as follows: PO (17, 14, 4% energy), OO (9, 21, 4% energy), SO (9.5, 12, 12.5% energy). The OO and SO diets were consumed for 5 weeks, while the PO diet was consumed for 4 weeks. Compared to the PO diet, the SO diet reduced TC by 18% and 12% in women and

men, respectively (P<0.001). LDL-C was reduced by 23% in women and 12.5% in men (P<0.001). The OO diet reduced TC by approximately 8% and LDL-C by 10% in both genders compared to the PO diet (P<0.001). HDL-C levels were not different between the diets and triglyceride levels were similar between diets with the exception that the SO diet reduced TG more in men versus the PO and OO diets. This trial demonstrates once again that replacing saturated fat with MUFA or PUFA in a moderate fat diet elicits favorable lipid profiles associated with reduced risk of CHD.

The hypocholesterolemic effect of unsaturated fats was demonstrated in a study by Binkoski et al (2005). Thirty-one men and women with moderately elevated cholesterol levels consumed three different diets in a cross-over design. The control diet was designed to reflect the average American diet containing 34% total fat and 11% saturated fat and the two test diets were Step 1 diets providing ~30% total fat and less than 10% saturated fat where olive or mid-oleic sunflower oil comprised 50% of the total fat content. Mid-oleic sunflower oil contains approximately 57% MUFA, 32% PUFA, and 9.6% SFA compared to 69% MUFA, 14% PUFA, and 14% SFA content of olive oil. Each diet was consumed for 4 weeks followed by a 2-week wash-out phase. The mid-oleic sunflower oil diet significantly lowered total (5.47 mmol/L) and LDL-C (3.54 mmol/L) compared to the average American (5.75 and 3.76 mmol/L) and olive oil (5.67 and 3.72 mmol/L) diets (P<0.05). Despite the fact that total fat was lower on the test diets, triglyceride levels did not differ between the three diets. No major differences were detected regarding markers of lipid oxidation

with the exception that lag time oxidation was increased 23% on the olive oil diet versus the mid-oleic sunflower diet. The greater cholesterol-lowering effect of the mid-oleic sunflower diet was attributed to the greater PUFA content. Furthermore, the authors suggest, that despite lowering SFA content on the olive oil diet, the total and LDL-C levels were not significantly affected because PUFA content was also lowered. They conclude that, rather than emphasizing MUFA sources over PUFA sources, foods that replace SFA should contain a balance of MUFA and PUFA.

The OmniHeart Trial (Appel 2005) was designed to test healthy diets on blood pressure and cholesterol levels. In a cross-over design, 164 subjects with hypertension or prehypertension consumed a diet low in total fat (27% en) and a diet enriched in MUFA from olive, canola and safflower oils (37% energy as total fat). The diets were comparable in SFA (6% energy) and PUFA (8-10% energy) content and contained similar amounts of protein (15% energy), fiber (>30 g/d), and cholesterol (<150 mg/d). The low-fat diet contained 13% energy from MUFA while the high MUFA diet contained 21% energy from MUFA. Compared to the low-fat diet, the high MUFA diet significantly lowered total (12 vs 15 mg/dl, $p<0.04$) non-HDL cholesterol levels (-11 vs -15%, $p<0.002$), and TG concentrations (0.1 vs -9%, $p<0.02$). LDL-C reductions were similar on the low-fat and high-MUFA diets (-12 vs -13%). Using the Framingham risk equation, partially replacing carbohydrates with predominantly MUFA reduced the risk of CHD by 19.6%. It is interesting to note, that compared to the low-fat diet, the high-MUFA diet significantly reduced systolic (-1.3 mmHg, $p<0.005$) and diastolic (-0.08, $p<0.02$) blood pressure.

The Womens' Health Initiative study (Howard et al, 2006) lends further support to the recommendations for moderate fat diets rich in unsaturated fats. In this study 48,835 women were examined to determine the health effects of consuming diets low in fat on incidence of CHD. The women in the Intervention group were instructed to reduce total fat intake to 20% of total calories and to consume 5 fruits/vegetables and 6 grain servings per day. The comparison group received diet-related educational materials. Most notable, after 6 years, was the fact that the women did not achieve 20% of energy from total fat though they did achieve what could be considered a low-fat diet. Participants in the intervention group reduced total fat intake by 8.2% (37.8% energy at baseline vs. 28.8% energy after 6 years). Small decreases were observed in saturated (2.9%), MUFA (3.5%) and PUFA (1.5%). Did not change percent sat fat……..Total fat intake for the comparison group remained steady at 37% of energy. The intervention diet had no impact on incidence of CHD, stroke or CVD compared to the comparison group. The key takeaway from this study is that simply reducing total fat intake did not substantially attenuate the risk of CHD. More targeted diet and lifestyle therapies included in current recommendations, including replacement of saturated and trans fats with unsaturated fats, are likely needed to lower risk.

C. OBSERVATIONAL STUDIES – UNSATURATED FATS

Numerous observational studies have reported inverse associations between MUFA and PUFA consumption and CHD risk. The Seven Countries Study found that increased MUFA intake was inversely associated (r = -0.42) with the 15-year death rate among 11,579 participants (Keys et al, 1986) and that PUFA intake was unrelated to CHD deaths. The Italian Nine Communities (Trevisan et al, 1990) study included 4,903 men and women aged 20-59 in which dietary fat intake was determined by interview-administered questionnaire. Higher consumption of butter and margarine was associated with elevated cholesterol levels, but the relationship was only statistically significant in men. Increased MUFA intake, primarily from olive oil, was associated with lower cholesterol levels in both men and women. Higher consumption of PUFA from vegetables oils (i.e. corn, soybean, sunflower oils) was also associated with lower blood cholesterol levels.

Ascherio (2002) reviewed the relationship between dietary fatty acids and CHD risk in the Health Professional Follow-up Study (HPFS) and the Nurses Health Study (NHS). Replacement of saturated fats with MUFA was associated with a 30% reduction in CHD risk which was determined to be 3-fold greater than replacing saturated fat with carbohydrate. In both studies, intake of linoleic and linolenic acids was inversely associated with risk of total and fatal CHD. A recent 20-year follow-up on the NHS found that saturated, MUFA, PUFA and trans fats were associated with CHD risk (Oh 2005). However, after multivariate analysis, only PUFA was inversely associated, and trans fat positively associated, with CHD risk. In addition, a spline analysis demonstrated a linear (inverse) relationship between increasing intakes of

PUFA and relative risk of CHD. PUFA intake and reduced risk of CHD was more apparent in overweight women (BMI>25) and the negative impact of trans fat on CHD risk was more apparent in younger women with a BMI less than 25.

Hu et al (2002) reviewed 147 studies relating to diet and CHD. Controlled clinical trials, metabolic ward studies, and epidemiological reports were considered though greatest weight was given to controlled clinical trials. Their findings reflect current dietary recommendations. In addition to increased consumption of n-3 fatty acids and a diet rich in fruit, vegetables, nuts and whole grains, replacing saturated and trans fats with MUFA and PUFA is a key strategy to reduce risk of CHD.

Most recently, Halton et al (2006) reviewed data from the Nurses' Health Study to determine the relationship between low-carbohydrate diets and the risk of CHD. Low-carbohydrate intakes were determined by percentage of total energy and given a score (10 points for lowest carbohydrate intake to 0 points for the highest carbohydrate intake). The points were then summed to arrive at the overall diet scores. Low-carbohydrate scores were then differentiated by percentage animal protein and fat vs plant protein and fat. During a 20 year follow-up 1,994 documented cases of CHD were recorded. Multivariate analyses determined that diets lower in carbohydrate and higher in protein and fat do not increase the risk for heart disease. Moreover, vegetable sources of fat and protein were associated with decreased risk in heart disease in women. The findings of this study are consistent with other population-based studies and support the findings of clinical feeding trials.

In conclusion, the studies reviewed herein, and those reviewed in the authoritative documents, consistently demonstrated that isocaloric replacement of saturated and trans fat or carbohydrate with unsaturated fats produced favorable changes in lipid profiles despite increased total fat intake. Specifically, while low-fat and moderate fat diets rich in unsaturated fats reduce total and LDL-C similarly, high carbohydrate intakes consistently reduce HDL cholesterol levels and increase triglyceride levels. Unsaturated fats maintain or increase HDL cholesterol levels and reduce TG compared to carbohydrate. While replacement of carbohydrate is not the focus of the proposed health claims for unsaturated fats and CHD, substantial evidence supports the conclusions of the authoritative bodies that the type of fat consumed is more important than the amount of fat consumed, given that total calories are controlled.

XII. ADDITIONAL SUPPORT FOR THE PROPOSED HEALTH CLAIMS

A. TOTAL FAT

In the past, the Dietary Guidelines for Americans (1990 – 1995) and many public health groups recommended low-fat (<30 percent total fat) diets to reduce blood lipid concentrations. However, in more recent years, authoritative bodies have determined that total fat intake, *per se*, is not directly linked to high blood cholesterol levels or CHD (*Diet and Health*, at 7; NCEP v-11; DRI Macronutrient Report). The ATP III Report states

> The major LDL-C-raising dietary constituents are saturated fat and cholesterol. A reduction in intakes of these components is the core of the TLC Diet.
>
> **Recommendation**: It is not necessary to restrict total fat intake for the express purpose of reducing LDL-C levels, provided saturated fatty acids are reduced to goal levels.

This recommendation is reflected in other guidelines. The 2000 and 2005 Dietary Guidelines for Americans no longer recommend low-fat diets, but rather that "fats should be chosen wisely" to keep saturated and trans fats and cholesterol intakes as low as possible. The Dietary Guidelines Advisory Committee Report provides rationale (Q1. DGAC Report) for the recommendation that total fat intake comprise 20-35 percent of total calories.

> The lower limit for fat intake is set at 20 percent of calories because serum triacylglycerol concentrations increase and serum HDL cholesterol concentrations decrease when fat intake is low and carbohydrate intake is high. This, in turn, may increase the risk of CHD. Furthermore, it is difficult to achieve recommended intakes of several nutrients when fat intake is below 20 percent of calories.
>
> The upper limit on total fat intake is related to the saturated-fat content of diets that provide more than 35 percent of calories from fat. Practical efforts to create heart-healthy menus that provide more than 35 percent of energy from total fat result in an unacceptably high content of saturated fatty acids. Because saturated fatty acids are present in all fats, higher intakes of total fat are associated with increased saturated fatty acid intakes.

The DRI Macronutrient Report (2002) concluded that total fat intake was not associated with incidence of CHD, but that diets exceeding 35 percent of total fat may provide excessive amounts of saturated fatty acids.

> Conclusions. A few case-control studies have shown an association between total fat intake and risk for CHD. However, a detailed evaluation of these

studies shows that it is not possible to separate total fat intake from saturated fatty acid intake, which is known to raise LDL-C concentrations. Unsaturated fatty acids, which do not raise LDL-C concentrations compared to carbohydrate, have not been implicated in risk for CHD through adverse effects on lipids or other risk factors. Nonetheless, practical efforts to create "heart-healthy" menus reveal that intakes of total fat exceeding 35 percent of total energy result in unacceptably high intakes of saturated fatty acids. Moreover, there is the possibility that higher fat intakes may enhance a prothrombotic state, although the evidence to support this mechanism for enhancing CHD risk is not strong enough alone to make solid recommendations. [Pages 801-02]

The relationship between dietary fats and cholesterol and the risk of heart disease is well established. The following are statements taken from authoritative bodies or reports from organizations that influence public nutrition policy.

B. SATURATED AND TRANS FATS

NCEP ATP III Report –

Evidence statements: *There is a dose response relationship between saturated fatty acids and LDL cholesterol levels. Diets high in saturated fatty acids raise serum LDL cholesterol levels (A1). Reduction in intakes of saturated fatty acids lowers LDL cholesterol levels (A1, B1). [Page V-8]*

Evidence statements: *High intakes of saturated fatty acids are associated with high population rates of CHD (C2). Reduction in intake of saturated fatty acids will reduce risk for CHD (A1, B1). [Page V-9]*

Evidence statements: *Trans fatty acids raise serum LDL cholesterol levels (A2). Through this mechanism, higher intakes of trans fatty acids should increase risk for CHD. Prospective studies support an association between higher intakes of trans fatty acids and CHD incidence (C2). [Page V-9]*

Dietary Guidelines Advisory Committee Report (2005)

Conclusion *The relationship between saturated fat intake and LDL cholesterol is direct and progressive, increasing the risk of cardiovascular disease (CVD). Thus, saturated fat consumption by adults should be as low as possible while consuming a*

diet that provides 20 to 35 percent calories from fat and meets recommendations for α-linolenic acid and linoleic acid. [Part D, Section 4, page 9]

***Conclusion**: The relationship between trans fatty acid intake and LDL cholesterol is direct and progressive, increasing the risk of CHD. Trans fatty acid consumption by all population groups should be kept as low as possible, which is about 1 percent of energy intake or less.* [Part D, Section 4, page 13]

American Heart Association 2006 Diet and Lifestyle Recommendations Revision

The AHA recommends intakes of <7% of energy as saturated fat, <1% of energy as trans fat, and <300 mg cholesterol per day. [Lichtenstein et al, 2006]

Diets low in saturated and trans fatty acids and cholesterol reduce the risk of CVD, in large part through their effects on LDL cholesterol levels. [Lichtenstein et al, 2006]

C. CHOLESTEROL

NCEP ATP III Report –

Evidence statements: Higher intakes of dietary cholesterol raise serum LDL cholesterol levels in humans (A2, B1). Through this mechanism, higher intakes of dietary cholesterol should raise the risk for CHD. Reducing cholesterol intakes from high to low decreases serum LDL cholesterol in most persons (A2, B1). [Page V-10]

Dietary Guidelines Advisory Committee Report (2005)

***Conclusion** The relationship between cholesterol intake and LDL cholesterol concentrations is direct and progressive, increasing the risk of CHD. Thus, cholesterol intake should be kept as low as possible, within a nutritionally adequate diet.*

D. MUFA and PUFA

Nutrition and Your Health: Dietary Guidelines for Americans, 1995

> *"Both kinds of unsaturated fats reduce blood cholesterol when they replace saturated fats in the diet."* [Page 29].
>
> *"Mono- and polyunsaturated fat sources should replace saturated fats within this limit."* [Page 29]

Dietary Guidelines Advisory Committee Report, 2000

> *"Dietary studies have demonstrated that both polyunsaturated and monounsaturated fats reduce LDL-cholesterol levels when they are substituted for saturated fats. Moreover, epidemiological studies have shown that populations that consume relatively high intakes of unsaturated fats, particularly monounsaturated fats, have low rates of both coronary heart disease and cancer. In addition, clinical trials strongly suggest that substitution of N-6 polyunsaturated fats for saturated fats reduces the risk for coronary heart disease."* [Page 36]
>
> *"Finally, with a "low-fat" recommendation, the potential benefit to be derived from the several forms of unsaturated fats may not be realized."* [Page 37]

Dietary Guidelines Advisory Committee Report, 2005

> ***Conclusion*** *An n-6 PUFA intake between 5 to 10 percent of energy may confer beneficial effects on coronary artery disease mortality. [Part D, Section 4, page 20]*
>
> ***Conclusion*** *There is an inverse relationship between the intake of MUFAs and the total cholesterol (TC):HDL cholesterol (HDL-C) concentration ratio. If equal amounts of MUFAs are substituted for saturated fatty acids, LDL-C decreases. [Part D, Section 4, page 29]*

FDA – [Speech before Harvard School of Public Health, Remarks by Mark B McClellan, MD, PhD Commissioner, Food and Drug Administration July 1, 2003]

> *"Let me give you a couple of examples of the kinds of health information that I'd like to see move from the academic journals to having an impact on the dietary choices of mainstream consumers. Considerable recent research, including controlled feeding and epidemiologic studies, has provided pretty good evidence that replacing saturated and trans fats with mono- and poly-unsaturated fats can significantly reduce important health risks. According to some studies, this substitution can potentially reduce the risk of heart disease by up to 30 to 40 percent. That is a big impact. But today, the labels on foods that are low in trans fats and, more importantly, that can reduce overall intake of trans and saturated fats in overall diet, can't disseminate this type of information to consumers. And so perhaps it's no surprise that many people don't have a clear understanding of the health consequences of their choices about mono- and polyunsaturated fats versus products high in saturated and trans fats. And it's no surprise that companies instead focus their marketing*

and their product development instead on whether a food is simply "low fat" and whether it springs ready to eat out of the box."

World Health Organization - The Joint WHO/FAO Expert Report Diet, Nutrition and the Prevention of Chronic Diseases (WHO 2003)

> *"When substituted for saturated fatty acids in metabolic studies, both monounsaturated fatty acids and n-6 polyunsaturated fatty acids lower plasma total and LDL cholesterol concentrations; PUFAs are somewhat more effective than monounsaturates in this respect. The only nutritionally important monounsaturated fatty acids is oleic acid, which is abundant in olive and canola oils and also in nuts. The most important polyunsaturated fatty acid is linoleic acid, which is abundant especially in soybean and sunflower oils. The most important n-3 PUFAs are eicosapentaenoic acid and docosahexaenoic acid found in fatty fish, and a-linolenic acid found in plant foods."* [Page 83]

Many of the statements in this section meet the requirements for an authoritative statement and, taken as a whole (including the authoritative statements presented to support the proposed health claims), all comments demonstrate the strength and pervasiveness of the evidence to support the proposed health claims for unsaturated fats and CHD. Most notably, the former FDA Commissioner not only acknowledged the strength of the evidence supporting the cardio-protective effects of substituting saturated and trans fats with MUFA and PUFA, but he also acknowledged consumer confusion regarding the health effects of unsaturated fats and called for clearer marketing communications. Without the proposed health claims, food manufacturers have little incentive and restricted means to inform the consumer about foods that can help substitute unsaturated fats for saturated fats in the diet.

XIII. REGULATORY PRECEDENT

The FDA relies on the Dietary Guidelines for Americans for rulemaking and therefore it is appropriate to highlight the statement from the 2005 Dietary Guidelines regarding dietary fats, which state that –

> *"Fats and oils are part of a healthful diet, but the type of fat makes a difference to heart health, and the total amount of fat consumed is also important. High intake of saturated fats, trans fats, and cholesterol increases the risk of unhealthy blood lipid levels, which, in turn, may increase the risk of coronary heart disease. A high intake of fat (greater than 35 percent of calories) generally increases saturated fat intake and makes it more difficult to avoid consuming excess calories. A low intake of fats and oils (less than 20 percent of calories) increases the risk of inadequate intakes of vitamin E and of essential fatty acids and may contribute to unfavorable changes in high-density lipoprotein (HDL) blood cholesterol and triglycerides." [Page 29]*

Regulatory precedent exists to support the criteria for the proposed health claims for unsaturated fat and reduced risk of heart disease. Until 2000, the Dietary Guidelines for Americans recommended low fat diets and the FDA therefore defined healthy foods as those low in total fat. However, since the release of the 2000 and 2005 Dietary Guidelines, FDA has acknowledged that "low-fat" was not requisite for a food to be "healthy". Both revisions of the Dietary Guidelines for Americans recommended diets moderate in total fat with the emphasis on keeping saturated and trans fat as low as possible. The FDA has used relaxed criteria regarding total fat in several health claims. Examples of the FDA rationale for this policy are provided below regarding plant sterol/stanol esters and CHD and the Olive Oil QHC. FDA also exercised this policy with respect to total fat in the soy and CHD health claim[33], the whole grains and CHD health claim[34] as well as qualified health claims for walnuts and CHD[35], nuts and CHD[36] and the Canola Oil QHC[37].

[33] 21 CFR §101.82

Plant Sterol/stanol Esters and CHD (21 CFR §101.83 and 65 Fed Reg at 54710)

The recently distributed Dietary Guidelines for Americans, 2000 modify the previous guideline for total fat intake. The new guideline states, "Choose a diet that is low in saturated fat and cholesterol and moderate in total fat." This new guideline also states, "Some kinds of fat, especially saturated fats, increase the risk for coronary heart disease by raising the blood cholesterol. In contrast, unsaturated fats (found mainly in vegetable oils) do not increase blood cholesterol." This modification in the dietary guidelines, from the recommendation to choose a diet low in total fat in the 4th edition of the U.S. Dietary Guidelines to the recommendation to choose a diet moderate in total fat in the Dietary Guidelines for Americans, 2000 is based on current scientific evidence of the role of diet in CHD, which does not support assigning first priority to a diet low in total fat. The agency's reliance on dietary guidelines in this rulemaking and in previous health claim regulations is based on provisions of the 1990 amendments that direct FDA to issue health claim regulations that take into account the role of the nutrients in food in a way that will enhance the chances of consumers maintaining healthy dietary practices (see section 403(r)(3)(A) and (r)(3)(B) of the act (21 U.S.C. 343(r)(3)(A) and (r)(3)(B)), along with legislative history that mentions the role of health claims in encouraging Americans to eat balanced, healthful diets that meet federal government recommendations. The agency finds that not imposing a "low fat" requirement is consistent with the emphasis in the new Dietary Guidelines for Americans, 2000 on diets moderate in total fat.

MUFA from Olive Oil and CHD (Docket No. 2003Q-0559)

The MUFAs from olive oil and CHD qualified health claim will inform consumers that they may lower their risk of CHD by consuming MUFAs from olive oil and olive oil products in place of SFAs, 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 saturated fat and cholesterol intake since olive oil contains no cholesterol and less saturated fat than other fat sources. Olive oil is a plant food and does not contain cholesterol. Furthermore, FDA concurs with current dietary guidelines that consuming diets low in saturated fat and cholesterol 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 olive oil, vegetable oil spreads, dressings for salads, shortenings, and olive oil-containing foods that bear a MUFAs from olive oil and CHD qualified health claim meet the "low fat" criterion.

---

[34] http://www.cfsan.fda.gov/~dms/flgrain2.html

[35] http://www.cfsan.fda.gov/~dms/qhcnuts3.html

[36] http://www.cfsan.fda.gov/~dms/qhcnuts2.html

[37] http://www.cfsan.fda.gov/~dms/qhccanol.html

In light of FDA's reliance on the Dietary Guidelines for Americans and other dietary guidance, de-emphasis on total fat in the present health claim notification is apropos. No authoritative body or public health group currently recommends a diet low in fat. In fact, all public health reports described herein state that it is most important to limit saturated and trans fat intakes rather than total fat. Guidelines to limit saturated and trans fats will inherently limit total fat intakes because all fats and oils contain a mix of fatty acids including saturated fat. Therefore, foods higher in total fat will fit into a healthy diet moderate in total fat content and low in saturated fat and trans fats.

Enforcement discretion has also been used regarding saturated fat content. The FDA recognized in its response to the Olive Oil QHC that all oils contain a mix of saturated and unsaturated fatty acids and that a tablespoon of olive oil does not meet the definition of "low saturated fat" as specified in 21 CFR §101.62(c)(2). However, it was stated that the qualified health claim would provide consumers with information to help facilitate reductions in saturated fat and cholesterol, since olive oil contains no cholesterol and less saturated fat than other fat sources. Therefore, FDA's enforcement discretion stipulated that olive oil be exempt from the 50 gram criterion of the saturated fat disqualifier value, and that olive oil and olive oil-containing foods do not need to meet the definition of "low saturated fat" in order to bear the claim. However, products that exceed this saturated fat content must use a disclosure statement for this dietary constituent.

Given this rationale, and the fact that olive oil is higher in saturated fat than most other heart healthy oils eligible for the proposed health claims, it follows that all oils with less than 20 percent of total fat as saturated fat would meet the agency's expectations for saturated fat content as stated in the Olive Oil QHC. The DRI Macronutrient Report (2002), as noted previously, considers oils to be low in saturated fat if they contain no more than 20 percent saturated fat as consumption of these oils would maintain a low saturated fat diet (<7 percent energy) within total fat intake recommendations up to 35 percent of total calories. As well, the criteria as proposed would keep saturated fat content well below disqualifying levels (21 CFR §101.14(a)(4)). Therefore, all oils eligible for the proposed health claims will help consumers reduce saturated fat intakes (via healthy oil substitutions) even though oils and some oil-containing foods do not meet the definition of "low saturated fat". Finally, as provided in Section 403r(3)(A)(ii) of the FD&C Act, health claims based on authoritative statements need only comply with Sections 403(a),[38] 403r(2)(B)[39], and 201(n)[40]. Therefore, unlike health claims submitted under 21 §CFR 101.70, health claims based on authoritative statements are not subject to the 10% minimum

[38] A food shall be deemed to be misbranded— (a) If (1) its labeling is false or misleading in any particular, or (2) in the case of a food to which section 411 applies, its advertising is false or misleading in a material respect or its labeling is in violation of section 411(b)(2).

[39] If a claim described in subparagraph (1)(A) is made with respect to a nutrient in a food and the Secretary makes a determination that the food contains a nutrient at a level that increases to persons in the general population the risk of a disease or health related condition that is diet related, the label or labeling of such food shall contain, prominently and in immediate proximity to such claim, the following statement: ''See nutrition information for ---- content.'' The blank shall identify the nutrient associated with the increased disease or health-related condition risk. In making the determination described in this clause, the Secretary shall take into account the significance of the food in the total daily diet.

[40] In determining whether labeling is misleading, the agency shall take into account not only representations made about the product, but also the extent to which the labeling fails to reveal facts material in light of such representations or material with respect to consequences that may result from use of the product. The omission of material facts from the labeling of a food causes the product to be misbranded within the meaning of section 201(n) and 403(a)(1) of the act. FDA may require disclosure of material facts in labeling by rulemaking or by direct enforcement discretion.

nutrient content requirement in 21 CFR §101.14(e)(6). Further evidence that nutritive value, and therefore health claims, cannot be limited to six nutrients is evident in where the FDA has exercised flexibility regarding this requirement. This requirement was exempted or modified in the following health claims: Plant sterol and stanol esters and coronary heart disease[41], nuts and coronary heart disease[42], walnuts and coronary heart disease[43] and whole grains and coronary heart disease[44]. The rationale for this policy was based on the findings that such health claims would assist consumers in maintaining healthy dietary practices. With regards to the plant sterol and stanol esters and CHD health claim, it was determined that the 10% minimum nutrient content requirement was outweighed by the health importance of communicating the cholesterol-lowering benefits from consumption of plant sterol/stanol esters for oil-based spreads. In addition, though sterol and stanol ester containing foods are presently required to meet the 10% minimum nutrient content requirement, the FDA allows for food manufacturers to submit comments with supporting information or petition the agency to request an exception from this requirement if they wish to use the health claim. In the nuts and CHD qualified health claim, it was determined that although [walnuts] do not meet the minimum 10 percent nutrient content requirement, the FDA used enforcement discretion as to this requirement because the levels of protein and dietary fiber in walnuts are very close to the 10 percent level. In the Health Claim Notification of Frito-Lay, Inc. (Docket No 2005Q-0211) with regards to whole grains and CHD, it

[41] 21 §CFR 101.83
[42] http://www.cfsan.fda.gov/~dms/qhcnuts2.html
[43] http://www.cfsan.fda.gov/~dms/qhcnuts3.html
[44] http://www.cfsan.fda.gov/~dms/flgrains.html

was determined that whole grains are heart healthy beyond their fiber content and are not inherently good sources of the six required nutrients including dietary fiber (in many cases). Therefore the 10% minimum nutrient content requirement was not enforced such that dietary fiber is only required at the compliance levels per RACC for a whole grain-containing food. Finally, FDA stated with regards to olive oil and canola oil (including spreads, salad dressings and shortenings) that it believes that information to help consumers reduce saturated fat and cholesterol consumption would assist them in maintaining healthy dietary practices and thus waived the 10% minimum nutrient content requirement for these products. FDA did not include oil-containing foods in this exemption. Given the recommendation from the 2005 Dietary Guidelines to "limit intake of fats and oils high in saturated and/or trans fatty acids, and choose products low in such fats and oils" as well as consumer research (FDA, 2004; IFIC, 2006) to suggest that consumers do not know what foods contain healthy versus unhealthy oils, enforcement of this regulation would unduly limit the foods that could contribute to beneficial effects from bearing the proposed claims. Additionally, trans fat labeling regulations demonstrated that replacing trans fats with unsaturated fats reduces CHD risk and did not factor in nutrient density. The FDA's advisory opinion from the trans fat labeling regulations is firm evidence that the benefit of replacing saturated and trans fats with unsaturated fats outweighs minimum nutrient requirement. Foods labeled with the proposed health claims would assist consumers in maintaining healthy dietary practices, since the claims provide consumers with information to select products that have less saturated and

trans fats and more unsaturated fats while not increasing their total caloric intake, as stated in the Olive and Canola Oil QHCs.

In summary, FDA policy with respect to a variety of qualified and unqualified health claims indicates that food choices consistent with the Dietary Guidelines for Americans need not be low fat, low in saturated fat, or comply with the 10% minimum nutrient content requirement in order to ultimately assist consumers in making healthy dietary choices. Moreover, science continues to evolve. Since the inception of health claim regulations (58 FR, 2478) science has definitively shown that type of fat is more important than total fat and that nutritive value goes beyond vitamins A, C, iron, calcium, protein or fiber in a healthy and calorie-balanced diet. Foods identified in this notification as potentially eligible for the health claims all provide nutritional value directly from grains, vegetables, or fruits (in addition to the vegetable oils themselves) or are typically used in combination with such foods (e.g., salad dressings and fresh vegetables). In addition, the healthy oils contained in such foods are a primary source of essential fatty acids, vitamin E, and naturally occurring free and esterified phytosterols in the diet. Vitamin E is considered a "nutrient of concern" in the 2005 Dietary Guidelines for Americans, suggesting that children and adults are not meeting the recommended intakes for this nutrient. Furthermore, the 2005 Dietary Guidelines for Americans define "discretionary calories" as those that provide energy but little essential nutrition. Solid fat (saturated and trans fats) and sugar calories always need to be counted as discretionary calories. Conversely, vegetable oils are not considered to be part of the discretionary calorie allowance because they are a major source of the essential

fatty acids and vitamin E in the food pattern. Finally, FDA has acknowledged that the 10% minimum nutrient content requirement need not be universally applied for CHD-related health claims and has granted multiple exemptions to this requirement. The reduced risk of CHD that can result from the replacement of fats high in saturated and trans fats with vegetable oils high in unsaturated fats and low in saturated fats (no more than 20% saturated fat), cholesterol and have 0 grams of trans fat is in line with these prior agency positions.

XIV. SUMMARY AND CONCLUSIONS

This notification has outlined the scientific, regulatory, and legal basis for the present notification for health claims regarding unsaturated fats and reduced risk of heart disease. The health claims will serve to provide consumers with information from several authoritative documents to assist them in making healthy dietary choices. While many authoritative statements are presented in this notification, they all reflect significant scientific agreement that replacing saturated and trans fats with MUFA and PUFA lowers blood cholesterol levels, prevents increases in triglycerides, and reductions in HDL-cholesterol, and therefore reduce the risk of CHD as part of a healthy overall diet that keeps saturated and trans fats and cholesterol as low as possible within moderate fat intakes. Studies published after the authoritative reports continue support and strengthen existing scientific consensus.

Criteria proposed in this notification are in accordance with previously authorized health claims as well as general requirements for FDAMA and the FD&C Act.

Most importantly, use of the health claims will assist consumers in making healthy dietary choices and to maintain diets consistent with the Dietary Guidelines for Americans and will provide incentives for food manufacturers to formulate and reformulate foods with heart healthy oils. We appreciate FDA's consideration of this important notification, and look forward to availability of the proposed health claims after 120 days.

Respectfully,

Rocco Papalia

Sr. Vice President, Research and Development

Frito-Lay, Inc.

XV. Notification Citations

AOAC. Official Methods of Analysis of AOAC International. Gaithersburg, MD: AOAC International, 1990.

Appel L.J., Sacks F.M., Carey V.J., Obarzanek E. and others. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. *JAMA* 2005;294:2455-2464.

Ascherio A. Epidemiologic studies on dietary fats and coronary heart disease. *Am. J. Med*. 2002;113 Suppl 9B:9S-12S.

Ash M. and Dohlman E. Oil Crops Situation and Outlook Yearbook. Washington, DC: Economic Research Service, U.S. Department of Agriculture, 2005.

Baudet M.F. and Jacotot B. Dietary fats and lecithin-cholesterol acyltransferase activity in healthy humans. *Ann. Nutr. Metab* 1988;32:352-359.

Binkoski A.E., Kris-Etherton P.M., Wilson T.A., Mountain M.L., and Nicolosi R.J. Balance of unsaturated fatty acids is important to a cholesterol-lowering diet: comparison of mid-oleic sunflower oil and olive oil on cardiovascular disease risk factors. *J. Am. Diet. Assoc.* 2005;105:1080-1086.

Dietary Guidelines Advisory Committee and Agricultural Research Service. Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans. Washington, DC: U.S. Department of Agriculture, U.S. Department of Health and Human Services, 2000.

Dietary Guidelines Advisory Committee. Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans. Washington, DC: U.S. Department of Agriculture, U.S. Department of Health and Human Services, 2005.

FDA Center for Food Safety and Nutrition. Health and Diet Survey. Washington, DC, U.S. Food and Drug Administration, 2004.

FDA Task Force on Consumer Health Information for Better Nutrition. Task Force Final Report. Washington, DC: U.S. Food and Drug Administration, 2003.

Food and Nutrition Board, Institute of Medicine, and National Academy of Sciences. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids (Macronutrients). Washington, DC: National Academies Press, 2002.

Food and Nutrition Board, National Research Council, and National Academy of Sciences. Diet and Health: Implications for Reducing Chronic Disease Risk. Washington, DC: National Academy Press, 1989.

Grundy S.M. Stanol esters as a component of maximal dietary therapy in the National Cholesterol Education Program Adult Treatment Panel III report. *Am. J. Cardiol.* 2005;96:47D-50D.

Halton T.L., Willett W.C., Liu S., Manson J.E. and others. Low-carbohydrate-diet score and the risk of coronary heart disease in women. *N. Engl. J. Med.* 2006;355:1991-2002.

Hegsted D.M., Ausman L.M., Johnson J.A., and Dallal G.E. Dietary fat and serum lipids: an evaluation of the experimental data. *Am. J. Clin. Nutr.* 1993;57:875-883.

Howard B.V., Van H.L., Hsia J., Manson J.E. and others. Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA* 2006;295:655-666.

Hu F.B. and Willett W.C. Optimal diets for prevention of coronary heart disease. *JAMA* 2002;288:2569-2578.

IFIC Foundation. Food and Health Survey: Consumer Attitudes Toward Food, Nutrition & Health. Washington, DC: International Food Information Council, 2006.

Katan M.B., Grundy S.M., Jones P., Law M. and others. Efficacy and safety of plant stanols and sterols in the management of blood cholesterol levels. *Mayo Clin. Proc*. 2003;78:965-978.

Keys A., Menotti A., Karvonen M.J., Aravanis C. and others . The diet and 15-year death rate in the seven countries study. *Am. J. Epidemiol.* 1986;124:903-915.

Kris-Etherton P.M., Pearson T.A., Wan Y., Hargrove R.L. and others. High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. *Am. J. Clin. Nutr.* 1999;70:1009-1015.

Lichtenstein A.H., Ausman L.M., Jalbert S.M., and Schaefer E.J. Effects of different forms of dietary hydrogenated fats on serum lipoprotein cholesterol levels. *N. Engl. J. Med.* 1999;340:1933-1940.

Lichtenstein A.H., Appel L.J., Brands M., Carnethon M. and others. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation* 2006;114:82-96.

Mata P., Garrido J.A., Ordovas J.M., Blazquez E. and others. Effect of dietary monounsaturated fatty acids on plasma lipoproteins and apolipoproteins in women. *Am. J. Clin. Nutr.* 1992;56:77-83.

Mensink R.P., Zock P.L., Kester A.D., and Katan M.B. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am. J. Clin. Nutr.* 2003;77:1146-1155.

Montoya M.T., Porres A., Serrano S., Fruchart J.C. and others. Fatty acid saturation of the diet and plasma lipid concentrations, lipoprotein particle concentrations, and cholesterol efflux capacity. *Am. J. Clin. Nutr.* 2002;75:484-491.

National Cholesterol Education Program. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. NIH Publication No. 02-5215. Bethesda, MD: National Heart, Lung and Blood Institute, 2002.

Oh K., Hu F.B., Manson J.E., Stampfer M.J., and Willett W.C. Dietary fat intake and risk of coronary heart disease in women: 20 years of follow-up of the nurses' health study. *Am. J. Epidemiol.* 2005;161:672-679.

Phillips K.M., Ruggio D.M., Toivo J.I., Swank M.A., and Simpkins A.H. Free and esterified sterol composition of edible oils and fats. *J. Food Comp. Anal.* 2002;15:123-142.

Trevisan M., Krogh V., Freudenheim J., Blake A. and others. Consumption of olive oil, butter, and vegetable oils and coronary heart disease risk factors. The Research Group ATS-RF2 of the Italian National Research Council. *JAMA* 1990;263:688-692.

U.S. Department of Health and Human Services and U.S. Department of Agriculture. Nutrition and your health: dietary guidelines for Americans, 3rd edition. Home and Garden Bulletin No. 232. Washington, DC: U.S. Department of Agriculture, 1990.

U.S. Department of Health and Human Services and U.S. Department of Agriculture. Nutrition and your health: dietary guidelines for Americans, 4th edition. Home and Garden Bulletin No. 232. Washington, DC: U.S. Department of Agriculture, 1995.

U.S. Department of Health and Human Services. Healthy People 2010: Understanding and Improving Health. Washington, DC: U.S. Government Printing Office, 2000.

U.S. Department of Health and Human Services and U.S. Department of Agriculture. Dietary guidelines for Americans 2005. Washington, DC: U.S. Government Printing Office, 2005.

Vega-Lopez S., Ausman L.M., Jalbert S.M., Erkkila A.T., and A.H.Lichtenstein. Palm and partially hydrogenated soybean oils adversely alter lipoprotein profiles compared with soybean and canola oils in moderately hyperlipidemic subjects. *Am. J. Clin. Nutr.* 2006;84:54-62.

WHO. Diet, Nutrition and the Prevention of Chronic Diseases. Report of a Joint WHO/FAO Expert Consultation. WHO Technical Report Series 916 . Geneva: World Health Organization, Food and Agriculture Organization of the United Nations, 2003.