

CLAIM STATEMENTS FOR NATURAL PRODUCTS

THE UNITED STATES MARKET



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Guide dealing with claim statements applicable to finished natural products marketed in the United States - explains types of claim statements according to product categories; illustrates how one plant can have different uses (dietary supplement, food additive, cosmetic, etc.), and how claims are made according to the product's recommended or intended use; offers examples of acceptable claim statements for certain categories; links to the relevant regulations and guidance documents issued by United States Food and Drug Administration (FDA); and regulatory guidance to support claims; offers examples of acceptable and non-acceptable claims for a range of Peruvian exported natural products; includes example of an FDA Dietary Supplement Notification Letter.

Descriptors: Market Access, Import Regulations, Non Tariff Barriers, Labelling, Biodiversity, Organic Products.

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English, Spanish (separate editions)

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Sustainability Market Guides

This is part of a series of Sustainability Market Guides produced under ITC's Trade, Climate Change and Environment Programme (TCCEP), financed by the Government of Denmark.

The series aims to guide exporters, civil society and policymakers on trends and practical guidance about the growing market for sustainably produced goods and services.

For further information about this series and the TCCEP, please contact Alexander Kasterine at kasterine@intracen.org.

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Acronyms

AHPA	American Herbal Products Association
ANDA	Abbreviated New Drug Application
APHIS	Animal and Plant Health Inspection Service (USDA)
CFR	Code of Federal Regulations
DHA	Docosahexaenoic acid (an omega-3 fatty acid)
DSHEA	Dietary Supplement Health and Education Act of 1994
DSP	Dietary Supplement Product
DV	Daily Value
EPA	Environmental Protection Agency
EPA	Eicosapentaenoic Acid (an omega-3 fatty acid)
FDA	Food and Drug Administration (regulates GMPs and labelling)
FD&C Act	Federal Food, Drugs and Cosmetics Act
FPLA	Fair Packaging and Labeling Act (administered by both FDA and FTC)
FSIS	Food Safety and Inspection Service (USDA)
FTC	Federal Trade Commission (regulates advertising)
GRAS	Generally Recognized as Safe (food)
GRASE	Generally Recognized as Safe and Effective (medicine)
IND	Investigational New Drug Application
ITC	International Trade Centre
NCC	Nutrient Content Claim
NDA	New Drug Application
NDC	National Drug Code Number (for PDP of OTC drug product labels)
NDI	New Dietary Ingredient (for dietary supplement products)
NIH	National Institutes of Health (United States Department of Health & Human Services)
OASIS	<i>Operational and Administrative System for Import Support</i> (FDA)
OTC	Over-the-counter Drug Product
PDP	Principle Display Panel (of product label)
QHC	Qualified Health Claim
RACC	Reference Amount Customarily Consumed
RDI	Reference Daily Intake
Rx	Prescription Drug Product
SSA	Significant Scientific Agreement
TFM	Tentative Final Monograph (published in the <i>Federal Register</i> ; Final Monographs are published in <i>Code of Federal Regulations</i> (CFR))
UNCTAD	United Nations Conference on Trade and Development
USDA	United States Department of Agriculture

Executive summary

In the United States of America (United States), regulations determine the claim statement(s) that a company can make when marketing a finished natural product. Products often carry statements that claim the product promotes health, can combat disease, or is cleansing. These claims are subject to United States regulation and therefore important for exporters to understand and comply with. This publication provides exporters with hands on expert guidance on the issue and so will help avoid some of the pitfalls of getting into the United States market for natural products.

Section 1 explains the different types of claims statements according to the categories of product and the types of claims.

The categories of products discussed in this Guide are the following:

- Dietary supplement and health food products
- Non drug cosmetic products
- Over-the-counter (OTC) drug products,

Each category of product has different requirements for Good Manufacturing Practice (GMP), quality of the substance that is the subject of the claim, the levels of evidence necessary to support a claim statement, and listing or notification requirements, among other differences.

Claims fall into the following categories:

- Cleansing, beautifying, promoting attractiveness, or altering the appearance claims
- Disease claims
- Health claims
- Nutrient content claims
- Qualified health claims
- Special dietary and nutritional additive claims
- Structure / function claims

This guide describes in detail the types of claim statements permissible for different product categories marketed in the United States.

It is also possible that a single natural ingredient could be allowed for several different recommended uses depending on the finished product form, the quality standard and GMPs. Section 2 uses the example of Capsicum fruit to show how one plant has different uses (dietary supplement, food additive, cosmetic, active pharmaceutical ingredient, and self defence) and how claims are made according to the product's recommended or intended use.

It gives examples of acceptable claim statements for these categories, as well as links to the relevant regulations and guidance documents provided by the United States Food and Drug Administration (FDA), including some available in Spanish.

The guide highlights regulatory guidance on levels of evidence to support claims (sections 3 and 4) and gives detailed examples of acceptable and non-acceptable claims for a range of Peruvian exported natural products (section 5). Section 6 gives an example of an FDA Dietary Supplement Notification Letter.

1. Types of claim statements

In the United States, the claim statement(s) that may be made on the labelling of a finished natural product are determined by the regulatory framework that the product is subject to. The form of the product (e.g. herbal extract in capsule or tablet, juice drink, herbal tea or tincture, nutrition bar, spray, cream or gel, etc), its mode of administration (e.g. topical, oral, nasal, enteral) and its recommended use(s) will place it into a particular regulatory category such as dietary supplement product, drug or non-drug cosmetic product, food product, food for special dietary use, medical food product, and over-the-counter (OTC) drug product or prescription (Rx) drug product.

The types of acceptable claim statements are limited to certain types of products and in many cases to specific substances that are expressly listed in a regulation to be allowed under certain conditions. Each regulatory framework has different requirements for Good Manufacturing Practice (GMP), quality of the substance that is the subject of the claim, the levels of evidence necessary to support a claim statement, and listing or notification requirements, among other differences.

This chapter provides a summary of the main types of claim statements permissible for different types of natural products marketed in the United States. In general these include:

- **Cleansing, beautifying, promoting attractiveness, or altering the appearance claims** allowable for non-drug cosmetic products such as skin moisturizers (excluding sun-protection products), perfumes, lipsticks, fingernail polishes, eye and facial makeup preparations, shampoos (excluding anti-dandruff shampoos), permanent waves, hair colours, toothpastes (excluding fluoride anti-cavity toothpastes), and deodorants (excluding antiperspirant products).
- **Disease claims** allowable for certain OTC drug products and certain Rx drug products. A statement is a disease claim if it mentions a specific disease or class of diseases. For example, a claim that a product 'reduces the pain and stiffness associated with arthritis' would be a disease claim. A statement also is a disease claim if it implies that it has an effect on a specific disease or class of diseases by using descriptions of the disease state such as 'improves joint mobility and reduces inflammation (rheumatoid arthritis),' or 'relief of bronchospasm (asthma)'. For example, an allowable OTC disease claim for the natural product **Capsicum Oleoresin USP** (alcoholic extract of the dried ripe fruits of *Capsicum annum* var. *minimum* and small fruited varieties of *C. frutescens*; Fam. Solanaceae) is 'For the temporary relief of minor aches and pains of muscles and joints associated with simple backache, arthritis, strains, bruises and sprains'.
- **Health claims** allowable for certain dietary supplement products and certain food products are limited to claims about disease risk reduction, and cannot be claims about the diagnosis, cure, mitigation, or treatment of disease. Use of a health claim on a product label requires pre-marketing review, evaluation and authorization by FDA. For example, an allowable health claim is 'Soluble fibre from foods such as **Psyllium husk** (*Plantago ovata* Forssk; Fam. Plantaginaceae), as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. One serving of this product supplies X grams of soluble fibre from psyllium necessary per day to have this effect'.
- **Nutrient content claims** allowable for certain dietary supplement products and certain food products. These are statements that directly or by implication characterize the level of a nutrient. For example, allowable nutrient content claims include, among others, 'low fat,' 'high in **antioxidant Vitamin C**,' or 'good source of fibre'.
- **Qualified health claims** allowable for certain dietary supplement products and certain food products. While 'Health claims' must meet the standard of Significant Scientific Agreement (SSA), certain 'Qualified health claims' are permissible based on less scientific evidence as long as the claims are qualified and do not mislead consumers. For example, an allowable qualified health claim is 'Supportive but not conclusive research shows that consumption of **EPA and DHA omega-3 fatty acids** may reduce the risk of coronary heart disease. One serving of this product provides X gram of EPA and DHA omega-3 fatty acids'.

- **Special dietary and nutritional additive claims** allowable for certain dietary supplement products and certain types of food products. For example, **Kelp** (the dehydrated, ground product prepared from *Macrocystis pyrifera* (L.) C. Aganth. (Fam. Lessoniaceae), *Laminaria digitata* (Huds.) J.V. Lamour., *Laminaria saccharina* (L.) Lamour., and/or *Laminaria cloustonii* Edmondston (Fam. Laminariaceae)) may be added to a food as a source of the essential mineral iodine, provided the maximum intake of the food as may be consumed during a period of one day, or as directed for use in the case of a dietary supplement, will not result in daily ingestion of the additive so as to provide a total amount of iodine in excess of 225 micrograms. Another example is **Folic acid** (folicin), which, under certain conditions, may be added to 'infant formula' products, or to 'medical foods' at levels not to exceed the amount necessary to meet the distinctive nutritional requirements of the disease or condition for which the food is formulated, or to 'foods for special dietary use' at levels not to exceed the amount necessary to meet the special dietary needs for which the food is formulated, and/or to foods represented as 'meal-replacement products'.
- **Structure / function claims** allowable for dietary supplement products and certain OTC drug products. Dietary supplement labels may bear statements that describe the role of a nutrient or dietary ingredient intended to affect the structure or function in humans or that characterize the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, provided that such statements are not disease claims. At the same time, many OTC drug monograph claims are also structure/function claim statements (and not disease claims). Thus, in certain cases an herbal dietary supplement product and an OTC herbal drug product could carry the very same claim statement. For example a stimulant laxative preparation based on **Senna leaf or pod** (*Cassia acutifolia* Delile or *C. angustifolia* Vahl; Fam. Fabaceae) may be labelled as either a dietary supplement product or as an OTC drug product, both with the same claim statement 'For the relief of occasional constipation (irregularity)'. While FDA ruled that inclusion of a claim in an OTC drug monograph does not preclude its use as a structure/function claim (for a dietary supplement product), FDA stated, that in light of the statutory requirement that dietary supplement labels bear all information that is 'material' (e.g. risk statements like cautions, contraindications and side effects), all material information contained in the referenced OTC monograph must also appear on the dietary supplement label.

It is also possible that a single natural ingredient could be allowed for several different recommended uses depending on the finished product form, the quality standard and GMPs. For example, Peru is an exporter of Organic and FairTrade Certified™ **Cocoa Butter** (fat obtained from the seed of *Theobroma cacao* L.; Fam. Sterculiaceae), which, in the United States, is permissible for use as a component of:

- (1) food products (e.g. in chocolate bars or ice cream);
- (2) dietary supplement products (e.g. in energy bars or protein bars);
- (3) non-drug cosmetic products (e.g. in skin moisturizing creams and lotions); and
- (4) OTC drug products (e.g. as a protectant active ingredient of haemorrhoidal drug products and/or as an active ingredient of lip or skin protectant drug products).

For further elaboration, please refer to section 2 of this report ('Food, Dietary Supplement or Drug Depending on the Claim Statement') which provides other examples of South American natural products that could bear different types of claim statements in the United States market depending on the type of product, recommended use(s), the quality of the component (e.g. food-grade or pharmaceutical quality) and the level of GMPs that were applied in the manufacture the product (e.g. cosmetic GMP, dietary supplement GMP, drug GMP, or food GMP).

1.1. Dietary supplement and health food products

As summarized in Chapter 1, a number of different types of claim statements may be permissible in the United States for the labelling of dietary supplement products and certain types of health food products such as foods with health claims, foods with qualified health claims, foods for special dietary use, and medical foods.

The following subsections provide further details and specific examples of acceptable claim statements for the main categories along with links to the corresponding regulations and guidance documents, some of which are available in Spanish language at the website of the United States Food and Drug Administration (FDA).

1.1.1. Health claims

FDA Guidance on Health Claims is available in Spanish language at:¹

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>

Health claim means any claim made on the label or in labelling of a food, including a dietary supplement, that expressly or by implication, including 'third party' references, written statements (e.g., a brand name including a term such as 'heart'), symbols (e.g., a heart symbol), or vignettes, characterizes the relationship of any substance to a disease or health-related condition. Implied health claims include those statements, symbols, vignettes, or other forms of communication that suggest, within the context in which they are presented, that a relationship exists between the presence or level of a substance in the food and a disease or health-related condition (see 21 CFR 101.14(a)(1)).²

Further, health claims are limited to claims about disease risk reduction, and cannot be claims about the diagnosis, cure, mitigation, or treatment of disease. Health claims are required to be reviewed and evaluated by FDA prior to use. Table 1 provides selected examples of specific health claim statements that have been authorized by the FDA.³

Table 1 Examples of acceptable authorized health claim statements

Approved claims	Requirements for the food	Claim requirements	Model claim statements
Fibre-Containing Grain Products, Fruits, and Vegetables and Cancer (21 CFR 101.76)	A grain product, fruit, or vegetable that contains dietary fibre; Low fat, and Good source of dietary fibre (without fortification).	Required terms: 'Fibre', 'Dietary fibre', or 'Total dietary fibre', 'Some types of cancer' or 'Some cancers', Does not specify types of dietary fibre that may be related to risk of cancer.	Low fat diets rich in fibre-containing grain products, fruits, and vegetables may reduce the risk of some types of cancer, a disease associated with many factors.
Fruits, Vegetables and Grain Products that contain Fibre, particularly Soluble Fibre, and Risk of Coronary Heart Disease (21 CFR 101.77)	A fruit, vegetable, or grain product that contains fibre; Low saturated fat, Low cholesterol, Low fat, At least 0.6 grams of soluble fibre per RACC (without fortification), and, Soluble fibre content provided on label.	Required terms: 'Fibre', 'Dietary fibre', 'Some types of dietary fibre', 'Some dietary fibres', or 'Some fibres'. 'Saturated fat' and 'Cholesterol'. 'Heart disease' or 'Coronary heart disease'. Includes physician statement ('Individuals with elevated blood total--or LDL--cholesterol should consult their physicians') if claim defines high or normal blood total--and LDL--cholesterol.	Diets low in saturated fat and cholesterol and rich in fruits, vegetables, and grain products that contain some types of dietary fibre, particularly soluble fibre, may reduce the risk of heart disease, a disease associated with many factors.

¹ Food and Drug Administration, 'Afirmaciones', *Guía para la industria: Guía de Etiquetado de Alimentos* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>.

² Food and Drug Administration, 'Health claims general requirements', *Code of Federal Regulations*, 21CFR §101.14 (Washington, D.C., United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-14.pdf>.

³ Food and Drug Administration, 'Appendix C: Health Claims', *Guidance for Industry: A Food Labeling Guide* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247932.htm>.

Approved claims	Requirements for the food	Claim requirements	Model claim statements
<p>Fruits and Vegetables and Cancer</p> <p>(21 CFR 101.78)</p>	<p>A fruit or vegetable, Low fat, and Good source (without fortification) of at least one of the following: Vitamin A, Vitamin C, or Dietary fibre.</p>	<p>Required terms:</p> <p>'Fibre', 'Dietary fibre', or 'Total dietary fibre';</p> <p>'Total fat' or 'Fat';</p> <p>'Some types of cancer' or 'Some cancers';</p> <p>Characterizes fruits and vegetables as 'Foods that are low in fat and may contain Vitamin A, Vitamin C, and dietary fibre';</p> <p>Characterizes specific food as a 'Good source' of one or more of the following: Dietary fibre, Vitamin A, or Vitamin C;</p> <p>Does not specify types of fats or fatty acids or types of dietary fibre that may be related to risk of cancer.</p>	<p>Low fat diets rich in fruits and vegetables (foods that are low in fat and may contain dietary fibre, Vitamin A, or Vitamin C) may reduce the risk of some types of cancer, a disease associated with many factors. Broccoli is high in vitamin A and C, and it is a good source of dietary fibre.</p>
<p>Soluble Fibre from Certain Foods and Risk of Coronary Heart Disease</p> <p>(21 CFR 101.81)</p>	<p>Low saturated fat, Low cholesterol, Low fat, and</p> <p>The food product must include one or more of the following whole oat or barley foods: 1) oat bran, 2) rolled oats, 3) whole oat flour, 4) whole grain barley or dry milled barley, and the whole oat or barley foods must contain at least 0.75 g of soluble fibre per RACC of the food product; or</p> <p>Oatrim that contains at least 0.75 g of beta-glucan soluble per RACC of the food product; or</p> <p>Psyllium husk that contains at least 1.7 g of soluble fibre per RACC of food product.</p> <p>Eligible Sources of Soluble Fibre</p> <p>Beta-glucan soluble fibre from the following whole oat and barley sources: 1) oat bran, 2) rolled oats, 3) whole oat flour, 4) oatrim, 5) whole grain barley and dry milled barley, 6) barley beta fibre, 7) soluble fibre from psyllium husk with purity of no less than 95%. The amount of soluble fibre per RACC must be declared in nutrition label.</p>	<p>Required terms:</p> <p>'Heart disease' or 'coronary heart disease';</p> <p>'Saturated fat' and 'cholesterol';</p> <p>In specifying the substance the claim uses the term 'soluble fibre' qualified by the name of the eligible source of the soluble fibre, which is either whole oat or barley or psyllium seed husk;</p> <p>Claim specifies the daily dietary intake of the soluble fibre source necessary to reduce the risk of CHD;</p> <p>Claim specifies the amount of soluble fibre in one serving of the product.</p> <p>Additional Required Label Statement</p> <p>Foods bearing a psyllium seed husk health claim must also bear a label statement concerning the need to consume them with adequate amounts of fluids; e.g., 'NOTICE: This food should be eaten with at least a full glass of liquid. Eating this product without enough liquid may cause choking. Do not eat this product if you have difficulty in swallowing'.</p> <p>(21 CFR 101.17(f))</p>	<p>Soluble fibre from foods such as [name of soluble fibre source, and, if desired, name of food product], as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of [name of food product] supplies ___ grams of the [necessary daily dietary intake for the benefit] soluble fibre from [name of soluble fibre source] necessary per day to have this effect.</p>

Approved claims	Requirements for the food	Claim requirements	Model claim statements
<p>Soy Protein and Risk of Coronary Heart Disease <i>(21 CFR 101.82)</i></p>	<p>At least 6.25 g soy protein per RACC; Low saturated fat, Low cholesterol, and Low fat (except that foods made from whole soybeans that contain no fat in addition to that inherent in the whole soybean are exempt from the 'low fat' requirement).</p>	<p>Required terms: 'Heart disease' or 'coronary heart disease'; 'Soy protein'; 'Saturated fat' and 'cholesterol'; Claim specifies daily dietary intake levels of soy protein associated with reduced risk; Claim specifies amount of soy protein in a serving of food.</p>	<p>(1) 25 grams of soy protein a day, as part of a low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of [name of food] supplies ___ grams of soy protein. (2) Diets low in saturated fat and cholesterol that include 25 grams of soy protein a day may reduce the risk of heart disease. One serving of [name of food] provides ___ grams of soy protein.</p>
<p>Plant Sterol/stanol esters and Risk of Coronary Heart Disease <i>(21 CFR 101.83)</i></p>	<p>At least 0.65 g plant sterol esters per RACC of spreads and salad dressings, or At least 1.7 g plant stanol esters per RACC of spreads, salad dressings, snack bars, and dietary supplements. Low saturated fat, Low cholesterol, and Spreads and salad dressings that exceed 13 g fat per 50 g must bear the statement 'see nutrition information for fat content'. Salad dressings are exempted from the minimum 10% DV nutrient requirement (see General Criteria below).</p>	<p>Required terms: 'May' or 'might' reduce the risk of CHD; 'Heart disease' or 'coronary heart disease' 'Plant sterol esters' or 'plant stanol esters', except 'vegetable oil' may replace the term 'plant' if vegetable oil is the sole source of the sterol/stanol ester; Claim specifies plant sterol/stanol esters are part of a diet low in saturated fat and cholesterol; Claim does not attribute any degree of CHD risk reduction; Claim specifies the daily dietary intake of plant sterol or stanol esters necessary to reduce CHD risk, and the amount provided per serving; Claim specifies that plant sterol or stanol esters should be consumed with two different meals each a day.</p>	<p>(1) Foods containing at least 0.65 gram per of vegetable oil sterol esters, eaten twice a day with meals for a daily total intake of least 1.3 grams, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of [name of food] supplies ___ grams of vegetable oil sterol esters. (2) Diets low in saturated fat and cholesterol that include two servings of foods that provide a daily total of at least 3.4 grams of plant stanol esters in two meals may reduce the risk of heart disease. A serving of [name of food] supplies ___ grams of plant stanol esters.</p>

1.1.2. Qualified health claims

FDA Guidance on Qualified Health Claims (QHC) is available in Spanish language at:⁴

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>

FDA has acknowledged that consumers benefit from more information on food labels concerning diet and health. As part of this initiative, the agency established interim procedures whereby QHCs can be made not only for dietary supplements but for conventional foods as well. Moreover, past court decisions have clarified the need to provide for health claims based on less scientific evidence rather than just on the standard of Significant Scientific Agreement (SSA) as long as the claims do not mislead the consumers.

Table 2 provides selected examples of specific qualified health claim statements that have been accepted by the FDA, for example for corn oil, nuts, olive oil, omega-3 fatty acids, soy derivatives and tomatoes, among other natural products.⁵ The table does not include the 'factors for exercising enforcement discretion,' which is essential information to understand prior to labelling a product with a QHC and is available on-line at:

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247933.htm>

Table 2 Examples of acceptable qualified health claim statements

Qualified health claims	Eligible foods	Claim statements
<p>Omega-3 Fatty Acids & Coronary Heart Disease Docket No. 2003Q-0401 09/08/2004 enforcement discretion letter - Wellness Petition 09/08/2004 enforcement discretion letter - Market Petition</p>	<p>Conventional foods and dietary supplements that contain EPA and DHA omega-3 fatty acids.</p>	<p>Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. One serving of [Name of the food] provides [] gram of EPA and DHA omega-3 fatty acids. [See nutrition information for total fat, saturated fat, and cholesterol content.]</p> <p>Note: Dietary supplements may declare the amount of EPA and DHA per serving in 'Supplement Facts,' instead of making the declaration in the claim.</p>
<p>Nuts & Heart Disease Docket No. 2002P-0505 07/14/2003 enforcement discretion letter</p>	<p>(1) Whole or chopped nuts listed below that are raw, blanched, roasted, salted, and/or lightly coated and/or flavoured; any fat or carbohydrate added in the coating or flavouring must meet the 21 CFR 101.9(f)(1) definition of an insignificant amount.</p> <p>(2) Nut-containing products other than whole or chopped nuts that contain at least 11 g of one or more of the nuts listed below per RACC.</p> <p>(3) Types of nuts eligible for this claim are restricted to almonds, hazelnuts, peanuts, pecans, some</p>	<p>Scientific evidence suggests but does not prove that eating 1.5 ounces per day of most nuts [such as name of specific nut] as part of a diet low in saturated fat and cholesterol may reduce the risk of heart disease. [See nutrition information for fat content.]</p> <p>Note: The bracketed phrase naming a specific nut is optional. The bracketed fat content disclosure statement is applicable to a claim made for whole or chopped nuts, but not a claim made for nut-containing products.</p>

⁴ Food and Drug Administration, 'Afirmaciones', *Guía para la industria: Guía de Etiquetado de Alimentos* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>.

⁵ Food and Drug Administration, 'Appendix D: Qualified Health Claims', *Guidance for Industry: A Food Labeling Guide* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247933.htm>.

Qualified health claims	Eligible foods	Claim statements
	pine nuts, pistachio nuts, and walnuts. Types of nuts on which the health claim may be based is restricted to those nuts that were specifically included in the health claim petition, but that do not exceed 4 g saturated fat per 50 g of nuts.	
<p>Green Tea & Cancer Docket No. 2004Q-0083 06/30/2005 enforcement discretion letter</p>	Green tea and conventional foods and dietary supplements that contain green tea.	<p>(1) Two studies do not show that drinking green tea reduces the risk of breast cancer in women, but one weaker, more limited study suggests that drinking green tea may reduce this risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of breast cancer. or,</p> <p>(2) One weak and limited study does not show that drinking green tea reduces the risk of prostate cancer, but another weak and limited study suggests that drinking green tea may reduce this risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of prostate cancer.</p>
<p>Phosphatidylserine & Cognitive Dysfunction and Dementia Docket No. 2002P-0413 02/24/2003 enforcement discretion letter 05/13/2003 clarification letter 11/24/2004 updated letter</p>	Dietary supplements containing soy-derived phosphatidylserine.	<p>(1) Consumption of phosphatidylserine may reduce the risk of dementia in the elderly. Very limited and preliminary scientific research suggests that phosphatidylserine may reduce the risk of dementia in the elderly. FDA concludes that there is little scientific evidence supporting this claim. or,</p> <p>(2) Consumption of phosphatidylserine may reduce the risk of cognitive dysfunction in the elderly. Very limited and preliminary scientific research suggests that phosphatidylserine may reduce the risk of cognitive dysfunction in the elderly. FDA concludes that there is little scientific evidence supporting this claim.</p>
<p>Monounsaturated Fatty Acids From Olive Oil and Coronary Heart Disease Docket No. 2003Q-0559 11/01/2004 enforcement discretion letter</p>	<p>All products that are essentially pure olive oil and labelled as such (see * for definitions).</p> <p>Dressings for salads (i.e. salad dressings) that contain 6 g or more olive oil per Reference Amount Customarily Consumed (RACC), are low in cholesterol (21 CFR 101.62(d)(2)), and do not contain more than 4 g of saturated fat per 50 g.</p> <p>Vegetable oil spreads that contain 6 g or more olive oil per RACC, are low in cholesterol (21 CFR 101.62(d)(2)) and do not contain more than 4 g of saturated fat per RACC.</p> <p>Olive oil-containing foods that contain</p>	<p>Limited and not conclusive scientific evidence suggests that eating about 2 tablespoons (23 grams) of olive oil daily may reduce the risk of coronary heart disease due to the monounsaturated fat in olive oil. To achieve this possible benefit, olive oil is to replace a similar amount of saturated fat and not increase the total number of calories you eat in a day. One serving of this product contains [x] grams of olive oil.</p> <p>Note: The last sentence of the claim 'One serving of this product contains [x] grams of olive oil' is optional when the claim is used on the label or in the labelling of olive oil.</p>

Qualified health claims	Eligible foods	Claim statements
	<p>6 g or more olive oil per RACC, are low in cholesterol (21 CFR 101.62(d)(2)), contain at least 10% of either vitamin A, vitamin C, iron, calcium, protein or dietary fibre. If the RACC of the olive oil-containing food is greater than 30 g the food cannot contain more than 4 g of saturated fat per RACC and if the RACC of the olive oil-containing food is 30 g or less the food cannot contain more than 4 g of saturated fat per 50 g.</p> <p>Shortenings that contain 6 g or more olive oil per RACC and are low in cholesterol (21 CFR 101.62(d)(2)) and do not contain more than 4 g of saturated fat per RACC.</p> <p>Meal products (21 CFR 101.13(l)) or Main dish products (21 CFR 101.13(m)) are not eligible for the claim.</p>	<p>*(1) Olive oil means virgin olive oil, or blends of virgin olive oil and refined olive oil; where virgin olive oil is the oil resulting from the first pressing of olives and is suitable for human consumption without further processing and refined olive oil is the oil obtained from subsequent pressings and which is suitable for human consumption by refining processes which neutralize the acidity or remove particulate matter.</p> <p>(2) Vegetable oil spread means margarine (21 CFR 166.110) and margarine-like products.</p> <p>(3) 'Dressings for salads' means dressings for salads formulated to contain olive oil.</p> <p>(4) 'Shortenings' means vegetable oil shortenings, formulated to contain olive oil.</p> <p>(5) Olive oil-containing foods means foods, such as sauces or baked goods, excluding olive oil, vegetable oil spreads, dressings for salads, and shortenings.</p>
<p>Tomatoes and/or Tomato Sauce & Prostate, Ovarian, Gastric, and Pancreatic Cancers</p> <p>Docket No. 2004Q-0201 11/08/2005 enforcement discretion letter - American Longevity Petition 11/08/2005 enforcement discretion letter - Lycopene Health Claim Coalition Petition</p>	<p>Cooked, Raw, Dried, or Canned Tomatoes.</p> <p>Tomato Sauces that contain at least 8.37% salt-free tomato solids.</p>	<p>Tomatoes and/or Tomato Sauce and Prostate Cancer:</p> <p>Very limited and preliminary scientific research suggests that eating one-half to one cup of tomatoes and/or tomato sauce a week may reduce the risk of prostate cancer. FDA concludes that there is little scientific evidence supporting this claim.</p> <p>Tomato Sauce and Ovarian Cancer:</p> <p>One study suggests that consumption of tomato sauce two times per week may reduce the risk of ovarian cancer; while this same study shows that consumption of tomatoes or tomato juice had no effect on ovarian cancer risk. FDA concludes that it is highly uncertain that tomato sauce reduces the risk of ovarian cancer.</p> <p>Tomatoes and Gastric Cancer:</p> <p>Four studies did not show that tomato intake reduces the risk of gastric cancer, but three studies suggest that tomato intake may reduce this risk. Based on these studies, FDA concludes that it is unlikely that tomatoes reduce the risk of gastric cancer.</p> <p>Tomatoes and Pancreatic Cancer:</p> <p>One study suggests that consuming tomatoes does not reduce the risk of pancreatic cancer, but one weaker, more limited study suggests that</p>

Qualified health claims	Eligible foods	Claim statements
		<p>consuming tomatoes may reduce this risk. Based on these studies, FDA concludes that it is highly unlikely that tomatoes reduce the risk of pancreatic cancer.</p>
<p>Corn Oil and Corn Oil-Containing Products and a Reduced Risk of Heart Disease Docket No. 2006P-0243 3/26/2007 enforcement discretion letter</p>	<p>Corn oil (see * for definitions). Vegetable oil blends and shortenings that contain 4 g or more corn oil per RACC, are low in cholesterol (21 CFR 101.62(d)(2)), do not meet the cholesterol and sodium disqualifying levels (21 CFR 101.14(a)(4)), and do not contain more than 4 g of saturated fat per RACC. Dressings for salads (i.e. salad dressings) that contain 4 g or more corn oil per RACC, are low in cholesterol (21 CFR 101.62(d)(2)), meet the cholesterol and sodium disqualifying levels (21 CFR 101.14(a)(4)), and do not contain more than 4 g of saturated fat per 50 g. Vegetable oil spreads that contain 4 g or more corn oil per RACC, are low in cholesterol (21 CFR 101.62(d)(2)), do not meet the cholesterol and sodium disqualifying levels (21 CFR 101.14(a)(4)), contain at least 10% of either vitamin A, vitamin C, iron, calcium, protein or dietary fibre, and do not contain more than 4 g of saturated fat per RACC. Corn oil-containing foods that contain 4 g or more corn oil per RACC, are low in cholesterol (21 CFR 101.62(d)(2)), meet the cholesterol and sodium disqualifying levels (21 CFR 101.14(a)(4)), contain at least 10% of either vitamin A, vitamin C, iron, calcium, protein or dietary fibre. If the RACC of the corn oil-containing food is greater than 30 g, the food cannot contain more than 4 g of saturated fat per RACC, and if the RACC of the corn oil-containing food is 30 g or less, the food cannot contain more than 4 g of saturated fat per 50 g.</p>	<p>Very limited and preliminary scientific evidence suggests that eating about 1 tablespoon (16 grams) of corn oil daily may reduce the risk of heart disease due to the unsaturated fat content in corn oil. FDA concludes that there is little scientific evidence supporting this claim. To achieve this possible benefit, corn oil is to replace a similar amount of saturated fat and not increase the total number of calories you eat in a day. One serving of this product contains [x] grams of corn oil.</p> <p>*(1) 'corn oil' means products that are essentially pure corn oil and are labelled as such. (2) 'Vegetable oil blends' means a blend of two or more vegetable oils formulated to contain corn oil. (3) 'Vegetable oil spread' means margarine (21 CFR 166.110) and margarine-like products formulated to contain corn oil. (4) 'Dressings for salads' means dressings for salads formulated to contain corn oil. (5) 'Shortenings' means vegetable oil shortenings formulated to contain corn oil. (6) 'Corn oil-containing foods' means all other foods, such as sauces or baked goods, formulated to contain corn oil, excluding corn oil, vegetable oil blends, vegetable oil spreads, dressings for salads, and shortenings.</p>

1.1.3. Nutrient content claims

FDA Guidance on Nutrient Content Claims (NCC) is available in Spanish language at:⁶
<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>

An NCC is a claim on a food product label that directly or by implication characterizes the level of a nutrient in the food (e.g., 'low fat,' 'high in antioxidant Vitamin C,' 'good source of fibre,' 'high in oat bran,' or 'contains 100 calories'). Table 3 provides selected examples of NCCs that are accepted by the FDA under certain conditions. For the general principles of NCCs please refer to 21 CFR 101.13(b) and 21 CFR 101.13(a) at:⁷

<http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-13.pdf>

Table 3 Examples of acceptable nutrient content claim statements

Acceptable NCC	Requirement for use of claim
High in antioxidant vitamins C and E ⁸	<p>A nutrient content claim that characterizes the level of antioxidant nutrients present in a food may be used on the label or in the labelling of that food when:</p> <ol style="list-style-type: none"> (1) An RDI has been established for each of the nutrients; (2) The nutrients that are the subject of the claim have recognized antioxidant activity; that is, when there exists scientific evidence that, following absorption from the gastrointestinal tract, the substance participates in physiological, biochemical, or cellular processes that inactivate free radicals or prevent free radical-initiated chemical reactions; (3) The level of each nutrient that is the subject of the claim is sufficient to qualify for the § 101.54 (b), (c), or (e) claim (e.g., to bear the claim 'high in antioxidant vitamin C,' the product must contain 20% or more of the RDI for vitamin C). Beta-carotene may be a subject of the claim when the level of vitamin A present as beta-carotene in the food that bears the claim is sufficient to qualify for the claim. For example, for the claim 'good source of antioxidant beta-carotene,' 10% or more of the RDI for vitamin A must be present as beta-carotene per reference amount customarily consumed; and (4) The names of the nutrients that are the subject of the claim are included as part of the claim (e.g., 'high in antioxidant vitamins C and E'). Alternatively, when used as part of a nutrient content claim, the term 'antioxidant' or 'antioxidants' (as in 'high in antioxidants') may be linked by a symbol (e.g., an asterisk) that refers to the same symbol that appears elsewhere on the same panel of a product label followed by the name or names of the nutrients with recognized antioxidant activity. The list of nutrients shall appear in letters of a type size height no smaller than the larger of one-half of the type size of the largest nutrient content claim or 1/16 inch.
'Contains x grams of omega-3 fatty acids per serving' or 'Provides x g of omega-3 fatty acids' ⁹	<p>A manufacturer may make a statement about a nutrient for which there is no established daily value (DV) as long as the claim specifies only the amount of the nutrient per serving and does not implicitly characterize the level of the nutrient in the product. To use the words 'contains' or 'provides' for nutrients without DVs, the specific amount of the nutrient must be stated. The statements 'Contains x grams of omega-3 fatty acids per serving' or 'Provides x g of omega-3 fatty acids' are permitted. However, 'Contains omega-3 fatty acids' or 'Provides omega-3 fatty acids' (without the specific amount statement) would not be permitted. Such claims would be synonyms for a 'good source' claim which is not permitted for nutrients that do not have established DVs.</p>

⁶ Food and Drug Administration, 'Afirmaciones', *Guía para la industria: Guía de Etiquetado de Alimentos* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>.

⁷ Food and Drug Administration, 'Nutrient content claims – general principles', *Code of Federal Regulations*, 21CFR §101.13 (Washington, D.C., United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-13.pdf>.

⁸ *Ibid.*, 21CFR§101.54. Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-54.pdf>.

⁹ Food and Drug Administration, 'Claims', *Guidance for Industry: A Food Labeling Guide* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>.

1.1.4. Structure / function claims

FDA Guidance on Structure / Function Claims is available in Spanish language at:¹⁰

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>

Dietary supplement product (DSP) labels or labelling may bear statements that describe the role of a nutrient or dietary ingredient intended to affect the structure or function in humans or that characterize the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, provided that such statements are not disease claims. If the label or labelling of a product marketed as a dietary supplement bears a disease claim the product will be subject to regulation as a drug unless the claim is an authorized health claim for which the product qualifies. Table 4 provides selected examples of structure/function statements for DSPs that may be accepted by the FDA as well as examples of non-acceptable statements.¹¹

Such statements are permitted so long as all of the requirements of 21CFR §101.93¹² are met (e.g. FDA Notification Letter signed by the responsible person has been sent in triplicate to FDA within 30 days of marketing the product; the notifying firm has prepared a substantiation file written by a qualified person to support the claim statements with sufficient levels of evidence; the labelling includes the required disclaimer statement; label text placement and size requirements, etc) and the product is manufactured in a registered facility according to current Good Manufacturing Practices (GMP) for DSPs.¹³

Table 4 Examples of acceptable and non-acceptable structure/function claim statements for DSPs

Acceptable structure/function claim for DSP	Non-acceptable claim for DSP
'Laxative - for the relief of <u>occasional</u> constipation (irregularity)'.	'Laxative for relief of <u>chronic</u> constipation' (occasional constipation is not a disease but chronic constipation is a disease).
'Relief of occasional heartburn'; 'Relief of occasional acid indigestion'; 'Relief of sour stomach'; 'Relief of upset stomach'.	'Relief of heartburn'; 'Relief of acid indigestion' ('recurrent' or 'persistent' heartburn and acid indigestion can be hallmarks of significant illness, and are therefore disease claims).
'Digestive aid'; 'Helps promote digestion'; 'For relief of occasional mild indigestion'.	'For chronic indigestion'.
'Antigas'; 'For relief of gas and bloating'; 'Alleviates the symptoms referred to as gas'; 'Alleviates bloating'; 'Alleviates pressure'; 'Alleviates fullness' and 'Alleviates stuffed feeling'.	
'For the prevention and treatment of the nausea, vomiting, or dizziness associated with motion'; 'For ordinary morning sickness associated with pregnancy'.	'Reduces nausea associated with chemotherapy'; 'For severe morning sickness (Hyperemesis gravidarum)' (a disease because it is an extreme, persistent nausea and vomiting during pregnancy).
'Soothing to the stomach due to carminative (antispasmodic) properties'.	'Soothing to the stomach due to an anti-inflammatory effect on the gastrointestinal tract' (the term 'antispasmodic' is not closely associated with treatment or prevention of gastrointestinal disease while the term

¹⁰ Food and Drug Administration, 'Afirmaciones', *Guía para la industria: Guía de Etiquetado de Alimentos* (October 2009). Available at:

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247929.htm>.

¹¹ Food and Drug Administration, '21CFR Part 101, Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*, vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

¹² Food and Drug Administration, 'Certain types of statements for dietary supplements', *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

¹³ *Ibid.*, 21CFR §111. Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-part111.pdf>.

Acceptable structure/function claim for DSP	Non-acceptable claim for DSP
	'anti-inflammatory' is strongly associated with treatment of certain serious gastrointestinal diseases, and would constitute a disease claim).
'Helps to maintain cholesterol levels that are already within the normal range'.	'Lowers cholesterol' (however qualified, is an implied disease claim. Lowering cholesterol is inextricably linked in the public mind with treating elevated cholesterol and preventing heart disease); 'Promotes cholesterol clearance' (is an implied disease claim because it is directed at lowering cholesterol rather than maintaining levels already determined to be within a normal range)
'Night-time sleep aid'; 'For the relief of occasional sleeplessness'; 'Promotes relaxation'.	'Helps you fall asleep if you have difficulty falling asleep'; 'Helps to reduce difficulty falling asleep' (these are disease claims because, unless the context makes clear that the product is only for occasional sleeplessness, they imply treatment of insomnia).
'For relief of occasional simple nervous tension'; 'For nervousness due to common every day overwork and fatigue'; 'For a relaxed feeling'; 'For calming down and relaxing'; 'Gently soothe away the tension'; 'Calmative'; 'For resolving that irritability that ruins your day'; 'Helps you relax'; 'For restlessness, nervous irritability'; 'When you're under occasional stress, helps you work relaxed'; 'Supports mood'; 'Reduces stress and frustration'.	'For long-term or chronic mood changes'; 'For migraine headache'; 'For nervous tension headache' (headache is a disease); 'For depression' (depression is a psychiatric disease).
'Stimulant - for occasional fatigue and drowsiness'; 'Helps restore mental alertness or wakefulness when experiencing fatigue or drowsiness'.	'For chronic fatigue or daytime drowsiness' (these can be symptoms of chronic fatigue syndrome and narcolepsy, which are both diseases).
'Improves absentmindedness;' 'Supports normal mental function'	'For Alzheimer's Disease'
'Maintains healthy lung function'.	'Maintains healthy lungs in smokers' (would imply prevention of tobacco related lung cancer and chronic lung disease).
'Promotes joint health'; 'Helps support cartilage and joint function'.	'Reduces the pain and stiffness associated with arthritis'; 'Improves joint mobility and reduces joint inflammation and pain' (implies treatment for rheumatoid arthritis, a disease).
'For relief of minor pain'; 'For muscle pain following exercise'; 'For treatment and/or prevention of nocturnal leg muscle cramps, i.e., a condition of localized pain in the lower extremities usually occurring in middle life and beyond with no regular pattern concerning time or severity'.	'Relieves headache pain'; 'Relieves crushing chest pain (angina or heart attack)'; 'For treatment or prevention of joint pain (arthritis)'
'Promotes heart health'; 'Cardio health'; 'Helps maintain cardiovascular function and a healthy circulatory system'.	'Prevents irregular heartbeat' (arrhythmias) ;'Prevents heart attack'; 'Prevents shortness of breath, an enlarged heart, inability to exercise, generalized weakness, and edema' (implies prevention of congestive heart failure).
'Arouses or increases sexual desire and improves sexual performance'; 'For decreased sexual function associated with aging'.	'Helps restore sexual vigour, potency, and performance'; 'Improves performance, staying power, and sexual potency;' and 'builds virility and sexual potency' (these are disease claims because they use the term 'potency,' which implies treatment of impotence, a disease. If, however, these claims made clear that they were intended solely for decreased sexual function associated with aging, they could be acceptable structure/function claims).

Acceptable structure/function claim for DSP	Non-acceptable claim for DSP
'Supports a normal, healthy attitude during PMS'; 'For mild mood changes, cramps, and edema associated with the menstrual cycle'; 'For temporary water weight gain associated with the premenstrual cycle'.	'For severe depression associated with the menstrual cycle'.
'Supportive for menopausal women'; 'For hot flashes associated with menopause'.	'Prevents bone fragility in post-menopausal women'; 'Helps maintain normal bone density in post-menopausal women (implies treatment for osteoporosis, a disease).'
'Promotes healthy prostate function'; 'Helps maintain normal prostate function'.	'Helps relieve the symptoms of benign prostatic hypertrophy (BPH), e.g., urinary urgency and frequency, excessive urinating at night, and delayed urination'; 'Helps to maintain normal urine flow in men over 50 years old' (an implied disease claim because the average or 'normal' state in men over 50 years old is diminishing urine flow, in most cases due to BPH, so that the apparent 'maintenance' really represents a claim of improvement (treatment)).
'Use as a part of your weight loss plan'; 'Appetite suppressant'; 'For weight control'.	'Appetite suppressant treatment for obesity' (obesity is a disease and that obesity claims are not acceptable structure/ function claims. Being overweight, i.e., being more than one's ideal weight but less than obese, however, is not a disease).
'Supports the immune system'.	'Supports the body's antiviral capabilities' (represents a claim of treatment or prevention of a specific class of diseases, those caused by viruses (e.g., colds, hepatitis, or HIV infection)).
Note: There are no legal structure/function claim statements for any upper respiratory tract infections or inflammations, allergy, cold, cough, fever or flu symptoms.	'Anti-inflammatory'; 'Antitussive' (for relief of cough); 'Bronchodilator' (for relief of bronchospasm, a characteristic symptom of asthma); 'Demulcent' (soothes sore throat and cough); 'Dietary support during the cold and flu season'; 'Promotes general well-being during the cold and flu season' (both are disease claims because they imply that the product will prevent colds and flu or will mitigate the symptoms of those diseases); 'Expectorant' (treatment for a characteristic symptom of colds, flu, and bronchitis); 'For cold and flu symptoms'; 'Nasal decongestant' (for common cold); 'For relief of sneezing, runny nose, and itchy watery eyes caused by exposure to pollen or other allergens'; 'Relieves excessive secretions of the nose and eyes' (hay fever).

1.2. Non-drug cosmetic products

The Federal Food, Drug and Cosmetic Act (FD&C Act) defines cosmetics by their intended use, as 'articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body...for cleansing, beautifying, promoting attractiveness, or altering the appearance' [FD&C Act, sec. 201(i)]. Among the products included in this definition are skin moisturizers, perfumes, lipsticks, fingernail polishes, eye and facial makeup preparations, shampoos, permanent waves, hair colours, toothpastes, and deodorants, as well as any material intended for use as a component of a cosmetic product.

Some cosmetic products could appear to meet the definitions of both non-drug cosmetics and drug cosmetic. Non-drug cosmetics are claimed only to cleanse, beautify or promote attractiveness. For example, a normal shampoo is a non-drug cosmetic because its intended use is to cleanse the hair. However, an antidandruff shampoo product is a drug cosmetic because its intended use is to treat dandruff. Another example is toothpaste. Toothpaste for merely cleaning or whitening the teeth is a non-drug cosmetic while toothpaste that contains fluoride is a drug cosmetic for preventing cavities. Deodorants are non-drug cosmetics unless they also contain antiperspirants active ingredients. Skin moisturizers are non-drug cosmetic products unless the label bears sun-protection claims which would cause the product to become a drug product.

1.3. OTC drug products

In the United States, there are just a few biodiversity products (botanicals) that are classified by the Food and Drug Administration (FDA) as Generally Recognized as Safe and Effective (GRASE) for a specific over-the-counter (OTC) drug uses. The labelling standards monographs, which provide the permitted disease claim statements and/or structure/function claim statements are published in either a final monograph in the Code of Federal Regulations (CFR) or may appear in a Tentative Final Monograph (TFM) that has been published in the *Federal Register*.

Section 1.3.1. provides OTC drug claim statements for selected botanical active ingredients that are the subject of either a TFM or a final monograph and are produced in Latin America. In order to make this type of claim statement on the product label, the drug product must be manufactured in a registered drug manufacturing establishment under current Good Manufacturing Practices (GMP) for finished pharmaceuticals. The product should be listed with the FDA and should have a National Drug Code (NDC) assigned. The product labelling must include all of the information in the FDA monograph and correspond to drug labelling regulations for location, type size and boldness of information.

1.3.1. Disease treatment claims

Table 5 provides examples of botanical active ingredients that are produced in Latin America, which may carry over-the-counter (OTC) drug claim statements. In some cases OTC drug claim statements may be disease claim statements and in other cases they may be structure/function claim statements.

Table 5 Selected Latin American botanical active ingredients and OTC drug claim statements

Botanical OTC active ingredient	Approved OTC drug claim statement(s)
Capsicum Oleoresin USP: the alcoholic extract of the dried ripe fruits of <i>Capsicum annum</i> var. <i>minimum</i> and small fruited varieties of <i>C. frutescens</i> (Solanaceae). It contains not less than 8.0% of total capsaicins [capsaicin (C ₁₈ H ₂₇ NO ₃), dihydrocapsaicin (C ₁₈ H ₂₉ NO ₃), and nordihydrocapsaicin (C ₁₇ H ₂₇ NO ₃)].	For the temporary relief of minor aches and pains of muscles and joints associated with simple backache, arthritis, strains, bruises and sprains. ¹⁴
Cocoa Butter USP: the fat obtained from the seed of <i>Theobroma cacao</i> Linné (Fam. Sterculiaceae). The free fatty acids in 10.0 g of it require for neutralization not more than 5.0 mL of 0.10 N sodium hydroxide (1.4% as oleic acid).	<u>As active ingredient of fever blister products:</u> ¹⁵ Relieves dryness and softens cold sores and fever blisters. Softens crusts (scabs) associated with cold sores and fever blisters. <u>As active ingredient of haemorrhoidal products:</u> ¹⁶ For the temporary relief of: anorectal itching and discomfort associated with haemorrhoids, anorectal disorders, inflamed haemorrhoidal tissues, anorectal

¹⁴ Food and Drug Administration, '21 CFR Part 338—External Analgesic Drug Products for Over-the-Counter Human Use; Tentative Final Monograph', Notice of Proposed Rulemaking, *Federal Register*, vol. 48, No. 27 (8 February 1983). pp. 5852-5869.

¹⁵ *Ibid.*, vol.55, No. 21 (31 January 1990). pp. 3362-3383.

¹⁶ Food and Drug Administration, '21 CFR Part 346—Anorectal Drug Products for Over-the-Counter Human Use', *Code of Federal Regulations* (Washington, DC, National Archives and Records Administration, 11 April 2011).

Botanical OTC active ingredient	Approved OTC drug claim statement(s)
	<p>inflammation, the symptoms of perianal skin irritation. Temporarily forms a protective coating over inflamed tissues to help prevent drying of tissues.</p> <p>Temporarily protects: irritated areas, the inflamed, irritated anorectal surface to help make bowel movements less painful, the inflamed irritated anorectal surface from irritation and abrasion during bowel movement.</p> <p><i>As active ingredient of lip or skin protectant products:</i>¹⁷</p> <p>Helps prevent, temporarily protects and helps relieve chafed, chapped or cracked skin and lips.</p> <p>Helps prevent and protect from the drying effects of wind and cold weather.</p> <p>Temporarily protects minor: cuts, scrapes, burns.</p>
<p><i>Ipecac Oral Solution USP</i> prepared from <i>Ipecac USP</i>: the dried rhizome and roots of <i>Cephaelis acuminata</i> Karsten, or of <i>Cephaelis ipecacuanha</i> (Brotero) A. Richard (Fam. Rubiaceae). Ipecac yields not less than 2.0% of the total ether-soluble alkaloids of ipecac. Its content of emetine (C₂₉H₄₀N₂O₄) and cephaeline (C₂₈H₃₈N₂O₄) together is not less than 90.0% of the amount of the total ether-soluble alkaloids. The content of cephaeline varies from an amount equal to, to an amount not more than 2.5 times, the content of emetine.</p>	<p>Emetic for emergency use to cause vomiting in poisoning.¹⁸</p>
<p><i>Compound Benzoin Tincture USP</i>: is an alcoholic liquid extract prepared from a mixture of moderately coarsely powdered Benzoin USP with moderately coarsely powdered Aloe USP (dried latex of the leaves of <i>Aloe barbadensis</i> Miller (Curaçao Aloe) or of <i>Aloe ferox</i> Miller and hybrids of this species with <i>Aloe africana</i> Miller and <i>Aloe spicata</i>), Storax USP (balsam obtained from the trunk of <i>Liquidambar orientalis</i> Miller or of <i>Liquidambar styraciflua</i> Linné (American Storax)), Tolu Balsam USP (balsam obtained from <i>Myroxylon balsamum</i> (Linné) Harms), and alcohol.</p>	<p><i>Oral mucosal protectant:</i>¹⁹</p> <p>Forms a coating over a wound.</p> <p>Protects against further irritation.</p> <p>For temporary use to protect wounds caused by minor irritations or injury.</p> <p>For protecting recurring canker sores.</p>

2. Food, dietary supplement or drug depending on the claim statement

It is also possible that a single natural ingredient could be allowed for several different recommended uses depending on the finished product form, the quality standard and GMPs. For example, Peru is a manufacturer and exporter of dried capsicum fruit powder as well as extracts and oleoresins of capsicum fruit a.k.a. paprika oleoresin. Depending on the form, this Latin American botanical species can be used in every type of product, dietary supplement product, drug product, food product, and non-drug cosmetic product, as well as police use or self-defence as a less-than-lethal force weapon for incapacitating dangerous or violently resisting suspects. Table 6 shows the various different possible uses of capsicum fruit in the United States depending on the product form.

¹⁷ *Ibid.*, 21 CFR Part 347.

¹⁸ *Ibid.*, 21 CFR §201.308.

¹⁹ Food and Drug Administration, 'Oral Health Care Drug Products for Over-the-Counter Human Use; Amendment to Tentative Final Monograph to include OTC Relief of Oral Discomfort Drug Products', Notice of proposed rulemaking, *Federal Register*, vol. 56, No. 185 (24 September 1991). pp. 48302-48347.

Table 6 Capsicum fruit: dietary supplement, drug, food, and self-defence product

Type of product	Capsicum fruit form	Claim or purpose
Dietary Supplement Product	Powdered cayenne fruit, extract or oleoresin	'Supports digestive system function'; 'Stimulates gastric juice production to promote proper digestive function'; 'Promotes the secretion of gastric juices and peristalsis of the intestine'.
Drug Product	Capsicum Oleoresin USP	For the temporary relief of minor aches and pains of muscles and joints associated with simple backache, arthritis, strains, bruises and sprains.
Food Product	Paprika powder or Paprika Oleoresin	Colour additive and/or Flavouring agent (Spice, Natural seasoning, Flavouring).
Non-drug Cosmetic Product	Capsicum extract, juice or resin	Skin conditioning and Hair conditioning.
Self Defence Product	Oleoresin Capsicum (Pepper Spray)	For self defence or for police use to incapacitate dangerous or violently resisting suspects.

3. FDA guidance on levels of evidence to support claims

The Federal Food, Drug, and Cosmetic Act (FD& C Act) requires that a manufacturer of a dietary supplement making a nutritional deficiency, structure/function, or general well-being claim have substantiation that the claim is truthful and not misleading. The Food and Drug Administration (FDA) has published a guidance document entitled '*Guidance for Industry: Substantiation for Dietary Supplement Claims Made Under Section 403(r) (6) of the Federal Food, Drug, and Cosmetic Act*'. This guidance document is intended to describe the amount, type, and quality of evidence FDA recommends a manufacturer have to substantiate a claim. The guidance document is available at the FDA's website at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/ucm073200.htm>

4. FTC guidance on levels of evidence to support claims

The role of the Federal Trade Commission (FTCO, which enforces laws outlawing 'unfair or deceptive acts or practices,' is to ensure that consumers get accurate information about dietary supplement products (DSPs) so that they can make informed decisions about these products. The FTC and the Food and Drug Administration (FDA) work together under a long-standing liaison agreement governing the division of responsibilities between the two agencies. As applied to DSPs, the FDA has primary responsibility for claims on product labelling, including packaging, inserts, and other promotional materials distributed at the point of sale. The FTC has primary responsibility for claims in advertising, including print and broadcast ads, infomercials, catalogues, and similar direct marketing materials. Marketing on the Internet is subject to regulation in the same fashion as promotions through any other media. Because of their shared jurisdiction, the two agencies work closely to ensure that their enforcement efforts are consistent to the fullest extent feasible.

The FTC has published guidelines for levels of evidence to support claim statements for the advertising of DSPs (including website content) entitled '*Dietary Supplements: An Advertising Guide for Industry*,' which is available at the FTC's website at: <http://business.ftc.gov/documents/bus09-dietary-supplements-advertising-guide-industry.pdf>

5. Examples of acceptable and non-acceptable claims

This chapter provides examples of acceptable and non-acceptable product label claim statements specifically for certain prioritized Peruvian natural products (e.g. camu-camu or maca products). Explanations are provided for acceptability or non-acceptability with links to further examples and/or guidance text published by the regulatory agency. For example, the FDA publishes its 'Letters of Objection' and 'Warning Letters' that are sent to companies for violations including non-acceptable claim statements. These documents provide useful insight into the agency's interpretation and enforcement of regulations concerning statements that can be made on product labelling.

Additionally, this chapter looks at acceptable and non-acceptable advertising claim statements, which are regulated by the Federal Trade Commission (FTC), an agency that uses a different set of rules than those applied by the FDA for product labels. Nonetheless, it is very important to be aware that while the FTC considers website content to be 'advertising,' the FDA considers certain website content to be an 'extension of product labelling'. As of late, the FDA has been enforcing, in part, by review of website content which may need to meet the same requirements as required for product labelling text.

5.1. Camu-camu

Camu-camu (*Myrciaria dubia* (Kunth) McVaugh; Fam. Myrtaceae) is listed in the American Herbal Products Association's (AHPA) *Herbs of Commerce*²⁰ and various forms of the fruit occur as components of some herbal dietary supplement products in the United States market. Camu-camu fruit juice concentrates and powdered dried fruit are also used in health food and raw food products. The expressed juice of the fruit as well as extracts of the fruit and/or seeds may be found as components of non-drug cosmetic products.

For the use of camu-camu fruit as a component of a dietary supplement product that will carry a structure/function claim statement on the product label, no later than 30 days after the first marketing of the product, the manufacturer, packer, or distributor must submit a Notification Letter to FDA (a signed original and two copies) which includes the text of the structure/function statement among other required information. The notice must be signed by the company's responsible person who can certify the accuracy of the information presented and contained in the notice and also certify that the notifying firm has substantiation that the statement is truthful and not misleading.²¹

FDA does not 'approve' claim statements. However, if FDA objects to a claim statement the agency may send a Letter of Objection in response to the Notification Letter. Or through post-marketing surveillance (of product labels and websites) FDA may issue a Warning Letter if they determine that violative claim statements are being made. Warning Letters require immediate action.

Table 7 provides specific examples of notified claim statements for camu-camu products that FDA has not objected to, as well as violative claim statements that have earned warning letters. Reasons for the acceptability or non-acceptability of each example are provided.

²⁰ M. McGuffin, J.T. Kartesz, A.Y. Leung, A.O. Tucker (eds.), *American Herbal Products Association's Herbs of Commerce*, 2nd edition (Silver Spring, Maryland, American Herbal Products Association, 2000).

²¹ Food and Drug Administration, 'Certain types of statements for dietary supplements', *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

Table 7 Acceptable and non-acceptable claim statements for camu-camu dietary supplement products

Acceptable claim statements	
Claim statement(s)	Reason it is acceptable
<p>A natural food source of Vitamin C.</p> <p>Extensive research on Vitamin C, of which camu-camu is a natural source, suggests that camu-camu standardized to 8% Vitamin C promotes a healthy immune system and supports mood balance.</p> <p>Scientific research documents the effects of Vitamin C to promote a healthy immune system. Camu-camu, a superior food source of Vitamin C, has been noted clinically to have these effects.²²</p>	<p>The product may contain enough Vitamin C to make a nutrient content claim.</p> <p>FDA permits 'supports mood' type structure / function claims because in order to substantiate the claim it is not necessary to study the effects of the product on clinical depression (a disease). Instead it is quite possible to assess the effects of the product on mood changes that do not constitute clinical depression.</p> <p>FDA permits 'supports the immune system' type structure / function claims because a statement of support for the immune system, by itself, conveys no specific reference to disease treatment or prevention.²³</p>
Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
<p>Research has shown that Camu-camu is used to ward off viral infections.</p> <p>Research has indicated that Camu-camu provides natural protection from Colds and Flu.²⁴</p>	<p>Claims that a product 'supports the body's antiviral capabilities' or 'supports the body's ability to resist infection' are disease claims. Claims that imply that a product will prevent colds and flu or will mitigate the symptoms of those diseases are disease claims.²⁵</p> <p>These therapeutic claims for camu-camu establish that the product is a drug because it is intended for use in the cure, mitigation, treatment, or prevention of disease. The marketing of this product with these claims violates the Federal Food, Drug, and Cosmetic Act.²⁶</p>
<p>It (camu-camu + acai juice) is a natural cholesterol controller which helps to reduce bad cholesterol. 'Anti-inflammatory', 'Best natural anti-depressant', 'Fights herpes virus', 'Fights cataracts and glaucoma', 'Combats infertility'.²⁷</p>	<p>Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease are drugs. The therapeutic claims on the labelling, including website, establish that this product is intended to be used as a drug. The marketing of this products with these claims violates the Federal Food, Drug, and Cosmetic Act.</p>

²² V. Muller, FDA Notification Letter: Royal Camu (9 July 2004). Available at: <http://www.fda.gov/ohrms/dockets/dailys/04/aug04/081704/97s-0162-let14406-vol125.pdf>.

²³ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body', Final Rule, *Federal Register*, vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

²⁴ V.H. Francos, FDA Cyber Letter to Life Dynamics Technology concerning its Camu-camu claim statements, Ref. No. CL-07-HFS-810-256 (8 May 2007). Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/CyberLetters/ucm056948.pdf>.

²⁵ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*, vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

²⁶ V.H. Francos, FDA Cyber Letter issued to Life Dynamics Technology concerning its Camu-camu claim statements, Ref. No. CL-07-HFS-810-256 (8 May 2007). Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/CyberLetters/ucm056948.pdf>.

²⁷ E.R. Singleton, FDA Warning Letter issued to Universal Taste Inc. concerning claim statements for its juice product Organic Acai + Camu-Camu, FLA-09-21, (7 August 2009). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2009/ucm183392.htm>.

Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
<p>Camu-camu is an antidepressant.</p> <p>Camu-Camu, a fruit with the highest concentration of vitamin C of any plant.²⁸</p>	<p>Antidepressant is a disease claim. Depression is a condition that is not amenable to self-diagnosis and treatment by individuals who are not medical practitioners.</p> <p>The 'highest concentration' is an unsupported nutrient content claim because it characterizes the level of a nutrient of a type required to be in the labelling of food (vitamin C) by using the term 'highest concentration'. A nutrient content claim may be made only if the characterization of the level made in the claim uses terms which are defined by regulation. However, FDA has not defined the characterization 'highest concentration' by regulation. Therefore, this term may not be used in nutrient content claims.</p>

5.2. Extracto de maíz morado

Extract of the whole cob of Andean purple corn (*Zea mays* L. var. *subnigroviolacea* Yarchuk; Fam. Poaceae) occurs as a component of some herbal dietary supplement products in the United States market albeit with somewhat limited claim statements, for example 'an extract with naturally occurring c3g (cyanidin-3-b-glucose),²⁹ or 'currently being studied for their weight loss potential'.³⁰ There are also purple corn extract products sold in the United States market with labels and/or website content that presently make illegal disease claims (e.g. 'with anti-inflammatory and anti-carcinogenic properties' or 'reduces cholesterol and helps fight obesity') and/or unauthorized nutrient content claims (e.g. 'source of potent antioxidants').

Since this standardized extract of whole corn cob was not a dietary ingredient that was not marketed in the United States before 15 October 1994, it was subject to the New Dietary Ingredient (NDI) requirement for premarket notification.³¹ In July of 2011, FDA issued new guidance for industry on NDI notifications and related issues.³²

In February 2005, Rainforest Botanicals LLC (Miami, FL) submitted an NDI application to the FDA, describing the NDI as 'Purple corn extract (manufactured by Laboratorios Fitofarma E.I.R.L., Lima, Peru) is a solvent (water-alcohol) extract of the whole cobs (without the leaves) of a coloured type of *Zea mays* L. from Peru, which is known by the vernacular, 'maíz morado' or purple corn. The form of the extract is a water-soluble powder standardized to contain proanthocyanidins (procyanidonic value of 12), approximately 6% anthocyanins: and approximately 25% total phenolic compounds. The taste of the extract is neutral, the odour is characteristic, and the colour is a deep purple. The carrier for the extract is non-GMO maltodextrin'.³³

²⁸ A.E. Cruse, FDA Warning Letter issued to Reed's Inc. concerning claim statements for its camu-camu containing product Reed's Natural Energy Elixir, W/L 43-11 (19 May 2011). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm256632.htm>.

²⁹ Solgar® South American Purple Corn 550 mg Vegetable Capsules: <http://www.solgar.com/SolgarProducts/South-American-Purple-Corn-550-mg-Vegetable-Capsules.htm>.

³⁰ Shaklee® Cinch® 3-in-1-Boost™ Tablets: http://www.shaklee.com/pws/library/products/20347_talksheet.pdf.

³¹ Food and Drug Administration, 'Requirement for premarket notification', *Code of Federal Regulations*, 21CFR §190.6 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol3/pdf/CFR-2011-title21-vol3-sec190-6.pdf>.

³² Food and Drug Administration, *Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues* (College Park, Maryland, Food and Drug Administration, July 2011). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/ucm257563.htm#>.

³³ J. Ferreira, Purple Corn Extract NDI Application Submitted by Rainforest Botanicals LLC (January 2005). Available at: <http://www.fda.gov/ohrms/dockets/DOCKETS/95s0316/95s-0316-rpt0281-02-vol218.pdf>.

In July 2005, the FDA responded that the NDI application provided insufficient safety information and stated that introduction of the product into interstate commerce was prohibited.³⁴ August 2005, Rainforest Botanicals provided FDA with additional human safety data to support the NDI application.³⁵ December 2005, FDA acknowledged receipt of the additional safety data but published no finding or conclusion.³⁶

Assuming that purple corn extract's NDI status is resolved, its use as a component of a dietary supplement product that will carry a structure/function claim statement on the product label would still require submission of a Notification Letter, no later than 30 days after the first marketing of the product (a signed original and two copies), which includes the text of the structure/function statement among other required information. The notice must be signed by the company's responsible person who can certify the accuracy of the information presented and contained in the notice and also certify that the notifying firm has substantiation that the statement is truthful and not misleading.³⁷

FDA does not 'approve' claim statements. However, if FDA objects to a claim statement the agency may send a Letter of Objection in response to the Notification Letter. Or through post-marketing surveillance (of product labels and websites) FDA may issue a Warning Letter if they determine that violative claim statements are being made. Warning Letters require immediate action.

A search of FDA documents found that no Notification Letters have been filed for any dietary supplement products containing purple corn extract. Thus, no Letters of Objection have been sent by FDA to notifying firms.

Table 8 Acceptable and non-acceptable claim statements for purple corn extract dietary supplement products

Acceptable claim statements	
Claim statement(s)	Reason it is acceptable
An extract with naturally occurring c3g (cyanidin-3-b-glucose).	This could be an acceptable content claim statement if the amount of c3g per serving is quantified in the Supplement Facts box of the label.
Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
Source of potent antioxidants.	This would be an unauthorized nutrient content claim. Nutrient content claims using the term 'antioxidant' must also comply with the requirements listed in 21CFR §101.54(g). ³⁸ These requirements state, in part, that for a product to bear such a claim, a Recommended Daily Intake (RDI) must have been established for each of the nutrients that are the subject of the claim. No RDI has been established by FDA for purple corn extract. Presently beta-carotene, Vitamin C and Vitamin E are the only substances authorized for antioxidant claim statements.
With anti-inflammatory and anti-carcinogenic properties.	These are disease treatment terms.

³⁴ S. J. Walker, FDA response to Purple Corn Extract NDI Application (June 2005). Available at: <http://www.fda.gov/ohrms/dockets/DOCKETS/95s0316/95s-0316-rpt0281-01-vol218.pdf>.

³⁵ J. Ferriera, Purple Corn Extract NDI Application Submitted by Rainforest Botanicals LLC (August 2005). Available at: <http://www.fda.gov/ohrms/dockets/DOCKETS/95s0316/95s-0316-rpt0303-03-vol240.pdf>.

³⁶ S.J. Walker, FDA second response to Purple Corn Extract NDI Application (December 2005). Available at: <http://www.fda.gov/ohrms/dockets/dockets/95s0316/95s-0316-rpt0303-02-vol240.pdf>.

³⁷ Food and Drug Administration, 'Certain types of statements for dietary supplements' *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>

³⁸ *Ibid.*, 21CFR§101.54. Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-54.pdf>.

Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
Reduces cholesterol and helps fight obesity.	References to lowering cholesterol are implied disease claims (hypercholesterolemia). FDA has concluded however that an appropriate and acceptable structure/function claim for maintaining cholesterol would be 'helps to maintain cholesterol levels that are already within the normal range.' ³⁹ Being overweight, but less than obese, is not a disease while obesity is a disease. Obesity claims are not acceptable structure/function claims.

5.3. Lúcumá

Lúcumá (*Pouteria lúcumá* (Ruiz & Pavon) Kuntze; Fam. Sapotaceae) is not listed in the American Herbal Products Association's (AHPA) *Herbs of Commerce*,⁴⁰ which 'might' be an indication that it was not in United States commerce prior to 15 October 1994. While this suggests that lúcumá might be a New Dietary Ingredient (NDI) if it were used as a component of a dietary supplement product, lúcumá fruit is already marketed as a food flavour ingredient. For example, certified organic dried lúcumá fruit powder is labelled and marketed for use as a dessert ingredient, with recommended applications as a flavour component of smoothies, puddings, and ice creams or as a flour component of pies and pastries.

Regarding use of the fresh fruit as an unprocessed food, on 07 June 2011, the United States Department of Agriculture (USDA) published a notice informing the public of sanitary and phytosanitary standard-setting activities for lúcumá fruit of the Codex Alimentarius Commission, in accordance with section 491 of the Trade Agreements Act of 1979, as amended, and the Uruguay Round Agreements Act.⁴¹ The new Codex Regional Standard for Lúcumá (CODEX STAN 305-R - 2011) applies to the fruit of commercial varieties of lúcumá grown from the *Pouteria lúcumá* (R. y P.) species, of the *Sapotaceae* family, to be supplied fresh to the consumer, after preparation and packaging. Lúcumá for industrial processing are excluded.⁴²

For possible future use as an active ingredient of drug cosmetic products, researchers at Rutgers, the State University of New Jersey, have applied for a patent for the 'Preparation and Use of *Pouteria lúcumá* Extract' (from lúcumá nut oil), with claims including wound healing, enhancing tissue regeneration, promoting skin healing, reducing skin senescence, healing skin burns, reducing, eliminating or preventing a skin condition (acne, skin aging and wrinkled skin).⁴³ A product with these claim statements however would need FDA authorization through a New Drug Application (NDA) process.

A search of FDA documents found that no Notification Letters have been filed for any lúcumá -containing dietary supplement products. It appears that the use of lúcumá fruit in the United States is presently limited to food products. A review of the published literature also suggests that there may be insufficient levels of evidence available to support the use of lúcumá as a dietary supplement component with a specific structure/function claim statement. However, in a recent nutrient content study of various Peruvian roots,

³⁹ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register* vol. 65, No. 4 (6 January 2000). pp.1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

⁴⁰ M. McGuffin, J.T. Kartesz, A.Y. Leung, A.O. Tucker (eds.), *American Herbal Products Association's Herbs of Commerce*, 2nd edition (Silver Spring, Maryland, American Herbal Products Association, 2000).

⁴¹ United States Department of Agriculture, 'International Standard-setting Activities', *Federal Register*, vol. 76, No. 109 (7 June 2011). pp. 32933-32943. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2011-06-07/pdf/2011-13985.pdf>.

⁴² Codex Alimentarius Commission, Norma Regional del Codex para la Lúcumá, CODEX STAN 305R (2011). Available at: http://www.codexalimentarius.net/download/standards/11922/CXS_305Rs.pdf.

⁴³ European Patent Register, Preparation and Use of *Pouteria lúcumá* Extract, All documents: EP2352489. Available at: <https://register.epo.org/espacenet/application?number=EP09826784&lng=en&tab=doclist>.

fruits, tubers, cereals and pulses, lúcumá fruit showed the highest value of total dietary fibre. This might be an area of research that could be developed for a certain dietary fibre claim statements.⁴⁴

If a lúcumá-based dietary supplement product or health food product can be shown to meet the requirements as a 'good source of dietary fibre,'⁴⁵ certain health claim statements could be allowed on the product labelling. For example, (any) fruits that are low fat and also a good source of dietary fibre (without fortification) may make the following health claim statement:

*'Low fat diets rich in fibre-containing grain products, fruits, and vegetables may reduce the risk of some types of cancer, a disease associated with many factors'.*⁴⁶

Additionally, if the lúcumá product is low in cholesterol, as well as low in fat and saturated fat and also provides at least 0.6 grams of soluble fibre per Reference Amount Customarily Consumed (RACC) (without fortification), the label could possibly carry the following health claim statement:

*'Diets low in saturated fat and cholesterol and rich in fruits, vegetables, and grain products that contain some types of dietary fibre, particularly soluble fibre, may reduce the risk of heart disease, a disease associated with many factors'.*⁴⁷

5.4. Maca

Maca (*Lepidium meyenii* Walpers; Fam. Brassicaceae) is listed in the American Herbal Products Association's (AHPA) *Herbs of Commerce*⁴⁸ and various forms of the root (powdered dried root, dried and liquid extracts) occur as components of some herbal dietary supplement products in the United States market. It is also possible that some processed forms are found as components of non-drug cosmetic products. For example, extracts of the roots as well as the hydrolysate of the roots (derived by acid, enzyme or other method of hydrolysis) might be used as skin conditioning ingredients.

In recent years maca has unfortunately been caught up in several controversies including lawsuits and regulatory actions due to allegedly unsupported or illegal claim statements made in advertising and/or on the labels of products that contain maca. For example, the United States Federal Trade Commission (FTC) sued a company for making male-fertility advertising claims for its maca-containing product that were allegedly unsupported by scientific evidence. The government eventually lost this case in district court.⁴⁹ And the United States Food and Drug Administration (FDA) took actions against companies making disease treatment claims on their maca product labels. One company's violative disease treatment claims for its maca product were 'for male impotence, infertility and osteoporosis... for memory disorders ...,' and 'supplants hormone replacement therapy,'⁵⁰ while another company received warnings for the claim 'Maca powder has been used to help relieve the symptoms of chronic fatigue, depression'.⁵¹

⁴⁴ P. Glorio et al. 'Fibra dietaria en variedades peruanas de frutas, tubérculos, cereales y leguminosas', *Rev. Soc. Quím*, vol. 74, No. 1 (Peru, 2008). pp. 46-56. Available at: <http://www.scielo.org.pe/pdf/rsgp/v74n4/a06v74n1.pdf>.

⁴⁵ Food and Drug Administration, 'Nutrient content claims for 'good source,' 'high,' 'more,' and 'high potency',' *Code of Federal Regulations*, 21CFR§101.54 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-54.pdf>.

⁴⁶ Food and Drug Administration, 'Appendix C: Health Claims', *Guidance for Industry: A Food Labeling Guide* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247932.htm>.

⁴⁷ *Ibid.*

⁴⁸ M. McGuffin, J.T. Kartesz, A.Y. Leung, A.O. Tucker (eds.), *American Herbal Products Association's Herbs of Commerce*, 2nd edition (Silver Spring, Maryland, American Herbal Products Association, 2000).

⁴⁹ United States District Court, District of New Jersey, Federal Trade Commission (FTC) vs. LANE LABS-USA, INC., CARTILAGE CONSULTANTS, INC., corporations, and I. WILLIAM LANE and ANDREW J. LANE, individuals. Available at: <http://www.ftc.gov/os/caselist/9823558/memorandumordershowcause.pdf>.

⁵⁰ C.W. Sedgewick, FDA Warning Letter concerning the product Maca Manna. Lanexa, Kansas: Food and Drug Administration (7 June 2001). Available at: <http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/2001/UCM069765.pdf>.

⁵¹ E.R. Singleton, FDA Warning Letter issued to Universal Taste Inc. concerning claim statements for its product Scoops Plus Maca, FLA-09-21 (7 August 2009). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2009/ucm183392.htm>.

There have also been nationwide recalls of several maca-containing products because FDA classified them as ‘unapproved new drug products,’ for example, in one case because the tablets were tested and found to contain an undeclared prescription drug ingredient ‘tadalafil’.⁵² Another maca-containing product was the subject of a nationwide recall because the product was being marketed without a New Drug Application (NDA) or an Abbreviated New Drug Application (ANDA) while the product was found to contain undeclared steroids or steroid-like substances, making them unapproved new drugs.⁵³ The most recent nationwide recall of a maca-containing product was because it was being marketed without an NDA/ANDA and FDA laboratory analysis of the product found the undeclared presence of ‘Sulfoildenafil’ an analogue of sildenafil, which is an FDA approved drug used in the treatment of male erectile dysfunction. This caused the maca product to be removed from the market as an ‘unapproved new drug’.⁵⁴

Additionally, there have been cases of import refusals, for example of maca capsules exported by Peruvian companies being classified by FDA as ‘misbranded drugs’ and/or ‘unapproved new drug products’. For example, one FDA import refusal listed three separate violations: (1) The article appears to be a drug and fails to bear the proprietary or established name and/or name and quantity of each active ingredient; (2) It appears the drug or device is not included in a list required by Section 510(j), or a notice or other information respecting it was not provided as required by section 510(j) or 510(k); and (3) The article appears to be a new drug without an approved new drug application.⁵⁵

For the use of maca root as a component of a dietary supplement product that will carry a structure/function claim statement on the product label, no later than 30 days after the first marketing of the product, the manufacturer, packer, or distributor must submit a Notification Letter to FDA (a signed original and two copies) which includes the text of the structure/function statement among other required information. The notice must be signed by the company’s responsible person who can certify the accuracy of the information presented and contained in the notice and also certify that the notifying firm has substantiation that the statement is truthful and not misleading.⁵⁶

FDA does not ‘approve’ claim statements. However, if FDA objects to a claim statement the agency may send a Letter of Objection in response to the Notification Letter. Or through post-marketing surveillance (of product labels and websites) FDA may issue a Warning Letter if they determine that violative claim statements are being made. Warning Letters require immediate action. Table 9 provides specific examples of ‘notified’ claim statements for maca products that FDA has not (yet) objected to, as well as violative claim statements that have earned warning letters from FDA. Reasons for the acceptability or non-acceptability of each example are provided.

⁵² Food and Drug Administration, Nationwide recall of Vigor-Rx Capsules, Pharmaceutical Grade Dietary Supplement, FDA Enforcement Report (21 January 2004). Available at: <http://www.fda.gov/Safety/Recalls/EnforcementReports/2004/ucm120280.htm>.

⁵³ Food and Drug Administration, Nationwide recall of Mass Tabs Capsules, Ripped Tabs TR Tablets, and Ripped Tabs TR Capsules. FDA Enforcement Report (21 April 2010). Available at: <http://www.fda.gov/Safety/Recalls/EnforcementReports/ucm209385.htm>.

⁵⁴ Food and Drug Administration, Nationwide recall of DURO EXTEND Capsules, FDA Enforcement Report (23 March 2011). Available at: <http://www.fda.gov/Safety/Recalls/EnforcementReports/ucm248171.htm>.

⁵⁵ Food and Drug Administration, Import Refusal Report. Refusal Details as Recorded in OASIS by FDA for Refusal 427-7102642-6/1/1 (2 May 2008). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=427-7102642-6&DocId=1&LineId=1&SfxId=

⁵⁶ Food and Drug Administration, ‘Certain types of statements for dietary supplements’, *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

Table 9 Acceptable and non-acceptable claim statements for maca dietary supplement products

Acceptable claim statements	
Claim statement(s)	Reason it is acceptable
Anti-fatigue. ⁵⁷	Anti-fatigue can be an acceptable structure / function claim statement so long as the overall context of the label does not imply use of the product for 'chronic fatigue' which is a disease. 'Occasional fatigue' and drowsiness however are not characteristic of symptoms of a specific disease or class of diseases. FDA provides an example of an acceptable claim: 'to help restore mental alertness or wakefulness when experiencing fatigue or drowsiness.' ⁵⁸
The ideal dietary supplement for a natural boost. Promotes stamina and endurance. ⁵⁹	FDA states that claims like 'boosts stamina' are acceptable structure/function claims, because they do not refer to any disease. ⁶⁰
Promotes Healthy Sexual Appetite, Function & Fertility. ⁶¹ Alkaloids isolated from the maca root act upon the hypothalamus-pituitary axis, supporting and boosting energy levels and encouraging the production of sex hormones. ⁶² 'Scientists are studying maca's ability to support healthy sexual endurance, energy and performance. Used for centuries to support fertility in both genders of humans and animals'. ⁶³ 'For natural virility and stamina. Maca has been traditionally used for stamina and libido by the people of the Andes Mountains of Peru'. ⁶⁴	FDA provides the following guidance on claims of this type: 'Arouses or increases sexual desire and improves sexual performance' is an acceptable structure/function claim because it does not imply treatment of a disease.

⁵⁷ X. Sha, FDA Notification Letter for MACA™ CAVAL POWER CAPSULES (5 May 2003). Available at: <http://www.fda.gov/ohrms/dockets/dailys/03/dec03/121003/97s-0162-let11913-vol94.pdf>.

⁵⁸ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*, vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

⁵⁹ S.C. Rodriguez, FDA Notification Letter for Maca 500 mg (1 October 1998). Available at: <http://www.fda.gov/ohrms/dockets/dockets/97s0162/let2281.pdf>.

⁶⁰ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*, vol. 64, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

⁶¹ E. Smith, FDA Notification Letter for Pharma Maca (11 February 2003). Available at: <http://www.fda.gov/ohrms/dockets/dailys/03/Nov03/110303/97s-0162-let11425-vol88.pdf>.

⁶² R.C. Doster, FDA Notification Letter for ITI Man™ (15 August 2004). Available at: <http://www.fda.gov/ohrms/dockets/dailys/04/sep04/092804/97s-0162-let14526-vol127.pdf>.

⁶³ M. Joslin, FDA Notification Letter for Maca 500 mg. (27 February 2001). Available at: <http://www.fda.gov/ohrms/dockets/dailys/01/Jun01/060401/let7350.pdf>.

⁶⁴ D. Shur Trinke, FDA Notification Letter for Sundown Standardized Maca (30 March 2000). Available at: <http://www.fda.gov/ohrms/dockets/DAILY/00/jun00/060900/let5161.pdf>.

Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
'Use it to treat numerous problems and diseases ...male impotence, infertility and osteoporosis... for memory disorders', 'aids in correcting and preventing prostatitis'. 'Hormonal balance and rejuvenation (avoid HRT)', 'supplants hormone replacement therapy', 'increase bone density, combats osteoporosis', 'protects against vaginal infection', 'eradicates invasive pathogens', 'cancer preventing nutrients'.	These are not structure/function claims under Section 403(r)(6) of the Federal Food Drugs and Cosmetics Act (FD&C Act) and/or under Title 21 Code of Federal Regulations (21 CFR) Section §101.93(g), ⁶⁵ but instead are all <u>disease claims</u> . ⁶⁶
'Maca powder has been used to help relieve the symptoms of chronic fatigue, depression'. ⁶⁷	Depression is a psychiatric disease. Chronic fatigue or daytime drowsiness can be symptoms of chronic fatigue syndrome and narcolepsy (a sleep disorder that causes excessive sleepiness and frequent daytime sleep attacks), which are both diseases. Thus, this is not a structure/function claim but instead a <u>disease claim</u> . ⁶⁸
'Helps restore sexual vigour, potency, and performance', 'improves performance, staying power, and sexual potency', and 'builds virility and sexual potency'.	These are <u>disease claims</u> because they use the term 'potency,' which implies treatment of impotence, a disease. If, however, these claims made clear that they were intended solely for decreased sexual function associated with aging, they could be acceptable structure/function claims. ⁶⁹

5.5. Sacha inchi

Sacha inchi (*Plukenetia volubilis* L.; Fam. Euphorbiaceae), also known as 'Inca peanut' is not listed in the American Herbal Products Association's (AHPA) *Herbs of Commerce*,⁷⁰ which 'might' be an indication that it was not in United States commerce prior to 15 October 1994 (pre-DSHEA). While this suggests that sacha inchi seed oil could be classified as a New Dietary Ingredient (NDI) if it were used as a component of a dietary supplement product, it is already marketed as a component of some (non-notified) dietary supplement products (e.g. seed oil to take by the teaspoons). A search of FDA documents found that no Notification Letters have actually been filed for any sacha inchi-containing dietary supplement products. However a search of the Internet found a number of 'non-notified' sacha inchi products marketed in the United States that are labelled as dietary supplement products, some with possibly legal 'qualified health claim' statements but some clearly with illegal 'disease claim' statements.

Sachi inchi is also being marketed as a component of some food products (e.g. cold-pressed seed oil for use in salad dressings and for main dishes) and cosmetic products (e.g. skin and hair care products), respectively. There may be non-drug cosmetic products in the market that contain extracts of the seeds or seedcake (the residue obtained from the expression of oil from the seeds) used as skin conditioning ingredients or the expressed seed oil used for skin conditioning, emollient (softens and smoothes the skin) or humectant (holds and retains moisture) functions.

Nonetheless, there have been recent cases of import refusals of sacha inchi products exported by Peruvian companies classified by FDA as 'unapproved new drugs'. For example, one recent FDA import

⁶⁵ Food and Drug Administration, 'Certain types of statements for dietary supplements', *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

⁶⁶ C.W. Sedgewick, FDA Warning Letter concerning the product Maca Manna (7 June 2001). Available at: <http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/2001/UCM069765.pdf>.

⁶⁷ E.R. Singleton, FDA Warning Letter issued to Universal Taste Inc. concerning claim statements for its product Scoops Plus Maca (7 August 2009). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2009/ucm183392.htm>.

⁶⁸ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*, vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

⁶⁹ *Ibid*.

⁷⁰ M. McGuffin, J.T. Kartesz, A.Y. Leung, A.O. Tucker (eds.), *American Herbal Products Association's Herbs of Commerce*, 2nd edition (Silver Spring, Maryland, American Herbal Products Association, 2000).

refusal involved sacha inchi dietary supplement capsules that carried disease claims (e.g. claims for lowering cholesterol and cardiovascular disorders).⁷¹ Another FDA import refusal in 2011 listed four separate violations for a sacha inchi seed oil product: (1) Misbranding: The article appears to lack adequate directions for use; (2) Not listed: It appears the drug or device is not included in a list required by Section 510(j), or a notice or other information respecting it was not provided as required by section 510(j) or 510(k); (3) Unapproved: The article appears to be a new drug without an approved new drug application; and (4) Warnings: It appears to lack adequate warning against use in a pathological condition or by children where it may be dangerous to health or against an unsafe dose, method, administering duration, application, in manner/form, to protect users.⁷²

There might be a possibility for certain sachi inchi seed oil products to be labelled with a specific 'qualified health claim'. For example, if a sacha inchi dietary supplement product or health food product can be shown to meet the specified omega-3 fatty acids content requirements, the following 'qualified health claim' for 'omega-3 fatty acids and coronary heart disease' might be possible for the product label:

'Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. One serving of [name of product] provides [X] gram of EPA and DHA omega-3 fatty acids. [See nutrition information for total fat, saturated fat, and cholesterol content.] Note: Dietary supplements may declare the amount of EPA and DHA per serving in 'Supplement Facts,' instead of making the declaration in the claim'.⁷³

In any case, for the use of sacha inchi seed oil as a component of a dietary supplement product that will carry a structure/function claim statement on the product label, no later than 30 days after the first marketing of the product, the manufacturer, packer, or distributor must submit a Notification Letter to FDA (a signed original and two copies) which includes the text of the structure/function statement among other required information. The notice must be signed by the company's responsible person who can certify the accuracy of the information presented and contained in the notice and also certify that the notifying firm has substantiation that the statement is truthful and not misleading.⁷⁴

FDA does not 'approve' claim statements. However, if FDA objects to a claim statement the agency may send a Letter of Objection in response to the Notification Letter. Or through post-marketing surveillance (of product labels and websites) FDA may issue a Warning Letter if they determine that violative claim statements are being made. Warning Letters require immediate action.

Table 10 provides specific examples of potentially acceptable as well as violative claim statements (excerpted from company websites marketing sachi inchi dietary supplement products in the United States). Reasons for the acceptability or non-acceptability of each example are provided.

⁷¹ Food and Drug Administration, Import Refusal Report, Refusal Details as Recorded in OASIS by FDA for Refusal XXX-0174907-7/1/5 (18 May 2011). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=XXX-0174907-7&DocId=1&LineId=5&SfxId=

⁷² *Ibid.*, Refusal EB6-0427176-8/1/1 (10 January 2011). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=EB6-0427176-8&DocId=1&LineId=1&SfxId=

⁷³ Food and Drug Administration, 'Appendix D: Qualified Health Claims', *Guidance for Industry: A Food Labeling Guide* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247933.htm>.

⁷⁴ Food and Drug Administration, 'Certain types of statements for dietary supplements', *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

Table 10 Acceptable and non-acceptable claim statements for sachai dietary supplement products

Acceptable claim statements	
Claim statement(s)	Reason it is acceptable
Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. One serving of [Name of the food] provides [X] gram of EPA and DHA omega-3 fatty acids. [See nutrition information for total fat, saturated fat, and cholesterol content.] Note: Dietary supplements may declare the amount of EPA and DHA per serving in 'Supplement Facts,' instead of making the declaration in the claim.	Conventional foods and dietary supplements that contain EPA and DHA omega-3 fatty acids may be permitted to use this 'qualified health claim' statement. ⁷⁵
Helps maintain cholesterol levels that are already within the normal range.	FDA does not believe that claims concerning maintenance of normal cholesterol levels necessarily constitute implied disease claims. Although an elevated cholesterol level is a sign of hypercholesterolemia and an important risk factor for heart disease, a cholesterol level within the normal range is not a sign or risk factor for disease. Moreover, maintaining cholesterol levels within the normal range is essential to the structure and function of the body for reasons other than prevention of heart disease. ⁷⁶
Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
'Controls and regulates the cholesterol and triglycerides improving the blood irrigation...' 'Can reduce levels of bad cholesterol in the blood and invigorates the heart, helps to reduce cardiovascular problems'. 'Cholesterol: Prevent blood clotting by keeping saturated fats mobile in the blood stream, helping to reduce the risk of coronary diseases'.	FDA continues to believe that 'lowers cholesterol,' however qualified, is an implied disease claim. Lowering cholesterol is inextricably linked with treating elevated cholesterol and preventing heart disease. The agency also believes that 'promotes cholesterol clearance' is an implied disease claim because it is directed at lowering cholesterol rather than maintaining levels already determined to be within a normal range. ⁷⁷ Such claims cause the product to be a 'new drug' without an approved new drug application (NDA). ⁷⁸
Act as antioxidant agent.	This would be an unauthorized nutrient content claim. Nutrient content claims using the term 'antioxidant' must also comply with the requirements listed in 21CFR §101.54(g). ⁷⁹ These requirements state, in part, that for a product to bear such a claim, a Recommended Daily Intake (RDI) must have been established for each of the nutrients that are the subject of the claim. No RDI has been established by FDA for sachai oil. Presently beta-carotene, Vitamin C and Vitamin E are the only substances authorized for antioxidant claim statements.

⁷⁵ Food and Drug Administration, 'Appendix D: Qualified Health Claims', *Guidance for Industry: A Food Labeling Guide* (October 2009). Available at: <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247933.htm>.

⁷⁶ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*, vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

⁷⁷ *Ibid.*

⁷⁸ Food and Drug Administration, Import Refusal Report, Refusal Details as Recorded in OASIS by FDA for Refusal XXX-0174907-7/1/5 (18 May 2011). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=XXX-0174907-7&DocId=1&LineId=5&SfxId=

⁷⁹ Food and Drug Administration, 'Nutrient content claims for 'good source', 'high', 'more', and 'high potency', *Code of Federal Regulations*, 21CFR§101.54 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-54.pdf>.

Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
Hypertension: Reduce triglycerides levels and hypertension.	Elevated blood pressure (hypertension) is a disease. Claims to reduce hypertension are disease claims.
Depression / Mental health: Regulate neural transmission and communication. Maintain the fluidity and rigidity of cellular membranes.	Depression is a disease condition that is not amenable to self-diagnosis and treatment by individuals who are not medical practitioners.
Arthritis: Reduce arterial inflammation.	Reduces joint inflammation and pain (rheumatoid arthritis) is a disease claim.
Diabetes / Weight loss: Regulate sugar levels in the blood.	Diabetes is a disease. By referring to the use of the dietary supplement in conjunction with and for the same purpose ('to maintain a healthy blood sugar level') as a drug (insulin), which is used to for a disease (diabetes), the statement implies that the dietary supplement will help treat diabetes. If the statement were changed to 'use as part of your diet to help maintain a healthy blood sugar level,' the claim would be considered acceptable. ⁸⁰
Control the symptoms of asthma in kids.	Treating asthma symptoms is a disease claim.

5.6. Sangre de grado

Sangre de grado (*Croton lechleri* Müll. Arg.; Fam. Euphorbiaceae) is listed in the American Herbal Products Association's (AHPA) *Herbs of Commerce*. Its standardized common name for labelling of products in the United States is 'dragon's blood croton'.⁸¹ The extract of the resin is found in a few (mostly non-notified) herbal dietary supplement products in the United States market. It may also be found as a skin conditioning component of some non-drug cosmetic products. In Canada, it is found as a non-medicinal ingredient (NMI) of just two licensed natural health products (NHP), both that contain salicylic acid as the sole active ingredient (e.g. a face wash gel for acne prone skin and a post-shave lotion to help prevent new acne breakouts).

Mainly, however, purified extractives of sangre de grado are destined for drug approval in the United States and other countries. 'Crofelemer,' a purified proanthocyanidin oligomer extracted from the bark latex of *Croton lechleri*, as an investigational new drug (IND) has now been studied in several clinical trials with funding through the United States National Institutes of Health (NIH) for treatment of secretory diarrheas.^{82,83,84} To date, crofelemer has been found to be safe, with no serious side effects or interactions with other drugs. Because diarrheal diseases are so prevalent in developing countries, crofelemer is being considered for further study and use in up to 140 countries in the developing world. Additional steps include testing the drug in children and as a treatment for irritable bowel syndrome.⁸⁵

Regarding sangre de grado dietary supplement products (DSP) exported by Peruvian companies, there have been some import refusals because FDA assessed them to be 'unapproved new drugs'. For example, one FDA import refusal listed two violations for a sangre de grado resin product: (1) Misbranded / Not listed: It appears the drug or device is not included in a list required by Section 510(j), or a notice or other information respecting it was not provided as required by section 510(j) or 510(k); and (2)

⁸⁰ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*. Vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

⁸¹ M. McGuffin, J.T. Kartesz, A.Y. Leung, A.O. Tucker (eds.), *American Herbal Products Association's Herbs of Commerce*, 2nd edition (Silver Spring, Maryland, American Herbal Products Association 2000).

⁸² L. Tradtrantip, W. Namkung, A.S. Verkman, 'Crofelemer, an Antisecretory Antidiarrheal Proanthocyanidin Oligomer Extracted from *Croton lechleri*, Targets Two Distinct Intestinal Chloride Channels', *Mol Pharmacol*, vol. 77 (January 2010). pp.69-78. Available at: <http://molpharm.aspetjournals.org/content/77/1/69.full.pdf>.

⁸³ R.D. Crutchley, J. Miller, K.W. Garey, 'Crofelemer, a Novel Agent for Treatment of Secretory Diarrhea' *Ann Pharmacother*, vol. 44, No. 5 (May 2010). pp. 878-884.

⁸⁴ United States National Institutes of Health, 'Crofelemer Clinical Trials. Bethesda'. Available at: <http://clinicaltrials.gov/ct2/results?term=crofelemer>.

⁸⁵ National Institute of Allergy and Infectious Diseases, 'A Possible New Drug to Treat Acute Diarrhea from Cholera and Other Conditions: Crofelemer' (22 June 2011). Available at: <http://www.niaid.nih.gov/topics/cholera/research/Pages/crofelemer.aspx>.

Unapproved: The article appears to be a new drug without an approved new drug application (NDA).⁸⁶ A more recent import refusal involved sangre de grado in the form of tablets packaged as a DSP, also refused entry into the United States by FDA because the product label claims caused it to be classified as an unapproved new drug.⁸⁷ Both products were likely labelled just as they are in Peru with disease claims such as 'Reduces inflammation, heals wounds, stop bleeding, and/or kills germs'.

For the use of dragon's blood croton as a component of a dietary supplement product that will carry a structure/function claim statement on the product label, no later than 30 days after the first marketing of the product, the manufacturer, packer, or distributor must submit a Notification Letter to FDA (a signed original and two copies) which includes the text of the structure/function statement among other required information. The notice must be signed by the company's responsible person who can certify the accuracy of the information presented and contained in the notice and also certify that the notifying firm has substantiation that the statement is truthful and not misleading.⁸⁸

FDA does not 'approve' claim statements. However, if FDA objects to a claim statement the agency may send a Letter of Objection in response to the Notification Letter. Or through post-marketing surveillance (of product labels and websites) FDA may issue a Warning Letter if they determine that violative claim statements are being made. Warning Letters require immediate action. Table 11 provides specific examples of notified claim statements for dragon's blood croton products that FDA has not objected to, as well as violative claim statements that FDA has objected to. Reasons for the acceptability or non-acceptability of each example are provided.

Table 11 Acceptable and non-acceptable claim statements for dragon's blood croton DSPs

Acceptable claim statements	
Claim statement(s)	Reason it is acceptable
Supports intestinal health. ⁸⁹	A claim to 'support' normal intestinal health is an acceptable structure / function claim statement. ⁹⁰
Promotes normal stool formation. ⁹¹	So long as the overall context of the claim(s) do not suggest or imply use for treatment of a disease (e.g. diarrhea), this claim, on its own, could be an acceptable structure / function claim statement.
Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
Controls diarrhea without causing constipation. A standardized extract from the sap of the Croton lechleri tree that has been used for centuries by shamans (traditional healers) in the Amazon rainforest to relieve diarrhea without causing constipation. Clinical studies demonstrated that this compound normalizes excess water flow in the intestinal tract and relieves diarrhea, without causing constipation.	Diarrhea is a disease. The statements suggest that the product is intended to treat, prevent, or mitigate disease, namely diarrhea. The claims not meet the requirements of 21 United States Codes Section 343 (21 U.S.C. 343(r)(6)). The claims suggest that this product is intended for use as a drug and that it is subject to regulation under the drug provisions of the Federal Food, Drug and Cosmetic Act (FD&C Act). ⁹²

⁸⁶ Food and Drug Administration, 'Import Refusal Report, Refusal Details as Recorded in OASIS by FDA for Refusal 110-0825533-3/1/1 (21 June 2002). Available at http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=110-0825533-3&DocId=1&LineId=1&SfxId=

⁸⁷ *Ibid.*, Refusal 900-0059056-3/1/21 (20 May 2010). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=900-0059056-3&DocId=1&LineId=21&SfxId=

⁸⁸ Food and Drug Administration, 'Certain types of statements for dietary supplements', *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

⁸⁹ J. Easterling, FDA Notification Letter for Amazon Herb Company Sangre De Drago Dietary Supplement (8 April 2003). Available at: <http://www.fda.gov/ohrms/dockets/dailys/03/dec03/120403/97s-0162-let11799-vol93.pdf>.

⁹⁰ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register* vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

⁹¹ L. Conte, FDA Notification Letter for SB-Normal Stool Formula (30 August 1999). Available at: <http://www.fda.gov/ohrms/dockets/dockets/97s0162/let4209.pdf>.

⁹² J.B. Foret, FDA Letter of Objection issued to Shaman Pharmaceuticals Inc. (2 October 2000). Available at: <http://www.fda.gov/ohrms/dockets/dailys/00/Nov00/110600/let0400.pdf>.

5.7. Uña de gato

Uña de gato (*Uncaria tomentosa* (Willd.) DC.; Fam. Rubiaceae) is listed in the American Herbal Products Association's (AHPA) *Herbs of Commerce*. Its standardized common name for labelling of products in the United States is 'cat's claw' (inner bark of stems).⁹³ Various forms of the stem bark (powdered bark, dried and liquid extracts) occur as components of dietary supplement products (DSP) in the United States market. It is also possible that some processed forms are found as components of non-drug cosmetic products. For example, powder or extracts of the stem bark might be used as skin conditioning ingredients. Cat's claw is not permitted as a component of conventional food products.

The United States Pharmacopeia (USP) has also established official quality standards for (1) Cat's Claw USP (inner bark of stems containing not less than 0.3% of pentacyclic oxindole alkaloids, calculated on the dried basis, as the sum of speciophylline, uncarine F, mitraphylline, isomitraphylline, pteropodine, and isopteropodine; and (2) Powdered Cat's Claw Extract USP (prepared from Cat's Claw USP by extraction with hydroalcoholic mixtures or other suitable solvents. The ratio of plant material to extract is between 4:1 and 6:1).⁹⁴ Use of the USP quality standards monographs as the basis of dietary supplement component specifications is voluntary unless the USP designation is made on the product label. If USP quality is claimed on the label then use of the USP standard becomes mandatory.

In recent years cat's claw has unfortunately been caught up in several controversies including numerous regulatory actions against companies due to unsupported or illegal claim statements made in advertising and/or on the labels of products that contain cat's claw (see table 12). For example, the United States Food and Drug Administration (FDA) has taken action against several companies making cancer treatment claims on their cat's claw product labels or website pages (web pages can be regulated as an extension of product labelling). In 2008, FDA sent Warning Letters to 28 United States companies and two foreign individuals marketing a wide range of products fraudulently claiming to prevent and cure cancer, several of which contained cat's claw bark or extract.⁹⁵ Such FDA warnings have resulted in some products being removed from the market entirely and/or some companies going out of business.

FDA warning letters have also been issued to companies for using cat's claw in products labelled as conventional food products. In one such case, FDA stated that it was not aware of any basis to conclude that uña de gato was the subject of a prior sanction or is generally recognized as safe (GRAS) for use in food products. Nor is uña de gato used in accordance with a food additive regulation. Thus, a conventional food product containing uña de gato is adulterated under section 402(a)(2)(C) of the Federal Food, Drug and Cosmetic Act (FD&C Act) and cannot be legally marketed in the United States.⁹⁶

Additionally, there have been cases of import refusals, for example of cat's claw bulk powder, cat's claw extract in glycerine soap and tinctures being classified by FDA as 'unapproved new drug products'. Two import refusals, one for a glycerine soap product with cat's claw extract⁹⁷ and another for a hydroalcoholic tincture product with cat's claw extract⁹⁸ were refused for the same reason: 'Unapproved New Drug: The article appears to be a new drug without an approved new drug application'. Another recent import refusal for bulk cat's claw bark powder was based on two violations: (1) Labelling / Misbranding: The article appears in violation of Fair Packaging and Labeling Act (FPLA)⁹⁹ because of its placement, form and/or

⁹³ M. McGuffin, J.T. Kartesz, A.Y. Leung, A.O. Tucker (eds.). *American Herbal Products Association's Herbs of Commerce*, 2nd edition (Silver Spring, Maryland, American Herbal Products Association, 2000).

⁹⁴ United States Pharmacopoeial Convention, Cat's Claw. United States Pharmacopeia 33rd Revision National Formulary 28th edition (USP33-NF28) (Rockville, Maryland, United States Pharmacopoeial Convention, 2010).

⁹⁵ Food and Drug Administration, Fake Cancer Cures (18 September 2008). Available at: <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/ucm073086.htm>.

⁹⁶ C.M. Breen, FDA Warning Letter issued to Herbal Junction (14 January 2004). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2004/ucm146137.htm>.

⁹⁷ Food and Drug Administration, Import Refusal Report, Refusal Details as Recorded in OASIS by FDA for Refusal XXX-0040521-8/1/1 (28 January 2002). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=XXX-0040521-8&DocId=1&LinId=1&SfxId=

⁹⁸ *Ibid.*, Refusal D99-3607164-3/7/1 (28 March 2011). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=D99-3607164-3&DocId=7&LinId=1&SfxId=

⁹⁹ Federal Trade Commission, *The Fair Packaging and Labeling Act* 15 U.S.C. §§1451-1461. Available at: <http://www.ftc.gov/os/statutes/fplajump.shtm>.

contents statement; and (2) Adulteration: The article appears to contain *Salmonella*, a poisonous and deleterious substance which may render it injurious to health.¹⁰⁰

For the use of cat's claw bark as a component of a DSP that will carry a structure/function claim statement on the product label, no later than 30 days after the first marketing of the product, the manufacturer, packer, or distributor must submit a Notification Letter to FDA (a signed original and two copies) which includes the text of the structure/function statement among other required information. The notice must be signed by the company's responsible person who can certify the accuracy of the information presented and contained in the notice and also certify that the notifying firm has substantiation that the statement is truthful and not misleading.¹⁰¹

FDA does not 'approve' claim statements. However, if FDA objects to a claim statement the agency may send a Letter of Objection in response to the Notification Letter. Or through post-marketing surveillance (of product labels and websites) FDA may issue a Warning Letter if they determine that violative claim statements are being made. Warning Letters require immediate action. Table 12 provides specific examples of 'notified' claim statements for cat's claw products that FDA has not (yet) objected to, as well as violative claim statements that have earned warning letters from FDA. Reasons for the acceptability or non-acceptability of each example are provided.

Table 12 Acceptable and non-acceptable claim statements for cat's claw bark DSPs

Acceptable claim statements	
Claim statement(s)	Reason it is acceptable
'For general health'; 'Supports healthy immune function'; 'Stimulates the immune system'. ¹⁰² 'Immune system herb'. ¹⁰³ 'It has been used traditionally to support healthy immune function and overall well-being'. ¹⁰⁴ '...helps to enhance natural immunity', '...helps to enhance the natural DNA repair process'. ¹⁰⁵ '...the tea (made of cat's claw) has strong influence and enhancement on human immune system...'. ¹⁰⁶ 'Patented and clinical studied to benefit the natural and acquired immune systems and enhances the protective power of critical B- and T- cells'. ¹⁰⁷	A statement of support for the immune system, by itself, conveys no specific reference to disease treatment or prevention. Claims to the effect of 'Supports the immune system' are not specific enough to imply prevention of disease.

¹⁰⁰ Food and Drug Administration, Import Refusal Report, Refusal Details as Recorded in OASIS by FDA for Refusal ALM-0802152-8/1/1 (28 June 2011). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=ALM-0802152-8&DocId=1&LineId=1&SfxId=

¹⁰¹ Food and Drug Administration, 'Certain types of statements for dietary supplements', *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

¹⁰² J. Easterling, FDA Notification Letter for Amazon Herb Company Uña de Gato (8 April 2003). Available at: <http://www.fda.gov/ohrms/dockets/dailys/03/dec03/120403/97s-0162-let11799-vol93.pdf>.

¹⁰³ T. Kimbell, FDA Notification Letter for BioEnergy Nutrients Uña de Gato GPH (10 December 1997). Available at: <http://www.fda.gov/ohrms/dockets/DOCKETS/97s0162/let0994.pdf>.

¹⁰⁴ D. Shur Trinker, FDA Notification Letter for Cat's Claw, (30 March 2000). Available at: <http://www.fda.gov/ohrms/dockets/DAILYS/00/jun00/060900/let5147.pdf>.

¹⁰⁵ H.M. Bayne, FDA Notification Letter for C-Med-100 (22 February 2000). Available at: <http://www.fda.gov/ohrms/dockets/dailys/00/jun00/060800/let5028.pdf>.

¹⁰⁶ R. Kafel, FDA Notification Letter for Cat's Claw Tea (27 September 2002). Available at: <http://www.fda.gov/ohrms/dockets/dailys/03/Sept03/092603/97s-0162-let11053-vol84.pdf>.

¹⁰⁷ R. Doster, FDA Notification Letter for Cell Forte® Max³, (23 December 2005). Available at: <http://www.fda.gov/ohrms/dockets/dockets/97s0162/97s-0162-let17140-vol155.pdf>.

Acceptable claim statements	
Claim statement(s)	Reason it is acceptable
'Supports joint health'; ¹⁰⁸ 'Musculoskeletal & joint support'; ¹⁰⁹ 'Supports structural health'. ¹¹⁰	Claims to the effect of 'Supports joint function' would be permissible structure/function claims, because they relate to maintaining normal function rather than treating joint pain. ¹¹¹
'Cat's Claw is a native Peruvian vine that is used to support the immune and digestive systems'. ¹¹² 'Supports normal cleansing of the intestinal tract and nutritionally supports the immune system'. ¹¹³	Immune system and digestive / gastrointestinal system support claims are acceptable structure/function statements because they are not specific enough to imply prevention or treatment of any disease.
'Researchers report that Cat's Claw may relax blood vessels, stimulate immune response, and promote neuromuscular wellbeing'. ¹¹⁴	So long as the overall context does not imply prevention or treatment of any specific disease, statements of promoting wellbeing and immune system support should be acceptable structure/function statements.

Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
'Cat's Claw ... From cancer and AIDS to the common cold, Cat's claw has proven effective for many people's needs'. ¹¹⁵	The claims make this product a 'drug' and/or a 'new drug'. A 'new drug' may not be introduced or delivered for introduction into interstate commerce unless an FDA-approved drug application is in effect for the drug.
'Antiviral'; 'Antirheumatic'; 'Uses: Rheumatism and arthritis. Gastritis and ulcers. As adjunct therapy in the treatment of cancer'. ¹¹⁶	The product is not generally recognized as safe and effective (GRASE) for the referenced conditions and therefore, the product is a 'new drug'. New drugs may not be legally marketed in the United States without prior approval from FDA.
(Implied) treatment for AIDS; (Implied) treatment for asthma. ¹¹⁷	The product is promoted for conditions that cause it to be a drug. The therapeutic claims on the web site establish that it is a drug because it is intended for use in the cure, mitigation, treatment, or prevention of disease. The marketing of this product with these claims violates the FD&C Act.
'used for arthritis, and some people find it beneficial to	This product is promoted for conditions that cause it to

¹⁰⁸ J. Easterling, FDA Notification Letter for Amazon Herb Company Uña de Gato (8 April 2003). Available at: <http://www.fda.gov/ohrms/dockets/dailys/03/dec03/120403/97s-0162-let11799-vol93.pdf>.

¹⁰⁹ A.K. Davis, FDA Notification Letter for MSM Musculoskeletal & Joint Support (22 March 2000). Available at: <http://www.fda.gov/ohrms/dockets/DAILY/00/jun00/060900/let5115.pdf>.

¹¹⁰ Neways Inc. FDA Notification Letter for Glucosamine Plus (24 February 2000). Available at: <http://www.fda.gov/ohrms/dockets/dailys/00/jun00/060800/let5023.pdf>.

¹¹¹ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*, vol. 64, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

¹¹² D. Metz, FDA Notification Letter for Cat's Claw Extract (24 November 1998). Available at: <http://www.fda.gov/ohrms/dockets/DOCKETS/97s0162/let2533.pdf>.

¹¹³ D. Bertrand, FDA Notification Letter for Cat's Claw (24 June 1998). Available at: <http://www.fda.gov/ohrms/dockets/DOCKETS/97s0162/let1746.pdf>.

¹¹⁴ I. Suarez, FDA Notification Letter for Cat's Claw powdered bark (12 May 1998). Available at: <http://www.fda.gov/ohrms/dockets/DOCKETS/97s0162/let1642.pdf>.

¹¹⁵ C.M. Breen, FDA Warning Letter issued to McAdam Health Enterprises (6 April 2006). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2006/ucm075859.htm>.

¹¹⁶ S.J. Walker, FDA Warning Letter issued to Vitamin Connection (28 March 2005). Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/CyberLetters/ucm059169.pdf>.

¹¹⁷ S.J. Walker, FDA Warning Letter issued to Herbal Nurse (22 September 2005). Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/CyberLetters/ucm059013.pdf>.

Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
use during cancer therapy'. ¹¹⁸	be a drug. The therapeutic claims on the web site establish that it is a drug because it is intended for use in the cure, mitigation, treatment, or prevention of disease. The marketing of this product with these claims violates the FD&C Act.
'The root and bark of Cat's Claw is used... for...arthritic conditions, asthma, cancer, fevers, ulcers, wounds'; 'Pharmacological Properties · anti-viral effect present against vesicular stomatitis virus in vitro · anti-inflammatory effect observed in laboratory animals ... · Austrian studies show anti-viral effects in humans. German studies showed a promise for leukemia...inhibits the proliferation of leukemic cells ...'. ¹¹⁹	FDA has no information that this product is generally recognized as safe and effective (GRASE) for the referenced conditions and therefore, this product may also be a 'new drug'. New drugs may not be legally marketed in the United States without prior approval from FDA.
'It helps to heal numerous stomach/intestinal disorders, including: Asthma, arthritis, ulcers, Chron's disease, diverticulitis, leaky bowel syndrome, colitis, gastritis, haemorrhoids, fistulas, liver disorders, parasites...'; 'Other conditions which might be treated with Cat's Claw include: arthritis and painful joints, rheumatism, cancer, bursitis, genital herpes, herpes roster, allergies, systemic candidiasis, ...HIV virus, environmental toxin poisoning...'. ¹²⁰	These claims cause the product to be a drug. New drugs may not be legally marketed in the United States without prior approval from FDA. Additionally, the claims on the labelling indicate the product is offered for conditions that are not amenable to self-diagnosis-and treatment by individuals who are not medical practitioners.
'A powerful combination of antioxidants and anti-inflammatories that help reduce stress and inflammation of the skin'; 'A uniquely formulated lotion that helps to reduce inflammation as well as minimize and potentially prevent bruising'; 'Can be used in conjunction with Post-Op to minimize scarring'. ¹²¹	This topical application product is an unapproved new drug. It does not conform to FDA's Tentative Final Monograph (TFM) for over-the-counter (OTC) External Analgesic drugs or to any other rulemaking under FDA's OTC Drug Review; it is not eligible for the OTC Drug Review; and it violates various provisions of the FD&C Act.
'An herb used to treat arthritis, gastritis, cancer, asthma, dermal and genito-urinary tract infections, and female hormone imbalances, as well as for other indications. ...for the treatment of rheumatism, genital herpes, ulcers, systemic candidiasis, organic depression, and HIV virus'. ¹²²	These claims cause this product to be a drug and also a 'New Drug' because there is no evidence that this product is generally recognized as safe and effective (GRASE) for its intended uses. Therefore, it may not be introduced or delivered for introduction into interstate commerce without an approved new drug application (NDA).
'Studies beginning in 1970 and continuing through today suggest it has applications in the treatment of cancer, arthritis, gastritis, ulcers, rheumatism ... organic depression, bursitis, genital herpes and herpes zoster, allergies, systematic candidiasis, diabetes, lupus, chronic fatigue syndrome ... numerous bowel and intestinal disorders and those infected with the HIV virus'. ¹²³	This product is not generally recognized as safe and effective (GRASE) for the referenced uses and, therefore, the product is a 'new drug'. New drugs may not be legally marketed in the United States without prior approval from FDA.

¹¹⁸ S.J. Walker, FDA Warning Letter issued to Beulah Land Nutritionals (6 Dec 2004). Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/CyberLetters/ucm056672.pdf>.

¹¹⁹ S.J. Walker, FDA Warning Letter issued to GCI Nutrients Worldwide Inc. (16 Feb 2005). Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/CyberLetters/ucm126468.pdf>.

¹²⁰ C.M. Breech, FDA Warning Letter issued to Alternative Health & Herbs Remedies (16 January 2007). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2007/ucm076245.htm>.

¹²¹ A.P. Reid, FDA Warning Letter issued to M W Laboratories Inc. (9 December 2009). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2009/ucm212634.htm>.

¹²² D.D. Tolen, FDA Warning Letter issued to Amazonic Herbals Inc. (13 December 1996). Available at: <http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/1996/UCM065152.pdf>.

¹²³ A.E. Cruse, FDA Warning Letter issued to NaturesAlternatives.com (02 June 2008). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2008/ucm1048264.htm>.

Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
'Cats Claw' is an herb used 'in the treatment of arthritis, gastritis, certain cancers, and other known epidemic diseases'. Your promotional material also offers Cats Claw for such serious conditions as 'Chron's [sic] disease, diverticulitis, recurring ulcers, and other intestinal conditions. The material further states that Cats Claw combats inflammation and tumour growth'. ¹²⁴	These claims cause the product to be a drug. It is a 'New Drug' and, therefore, may not be marketed in the United States without an approved new drug application (NDA) under the FD&C Act.
'Treatment for a wide range of health problems'; '...there is evidence to suggest that Uncaria Tomentosa may be beneficial in the treatment of cancer, arthritis, bursitis, rheumatism, herpes, ulcers, systemic candida ...many bowel and intestinal disorders, and those infected with HIV virus'; and 'its remarkable ability to cleanse the entire intestinal tract and help patients suffering from Chron's disease, diverticulitis, leaky bowel syndrome, colitis, haemorrhoids, gastritis, ulcers, parasites, yeast...'. ¹²⁵	These claims cause the product to be a drug. It is a 'New Drug' and, therefore, may not be marketed in the United States without an approved new drug application (NDA) the FD&C Act.
'...is helpful for a wide range of conditions, including Lyme Disease, arthritis, bursitis, cancer, rheumatism, allergies, ulcers, candida, herpes, diabetes, lupus and chronic fatigue syndrome'; '...can be used for Crohn's disease, haemorrhoids, parasites, leaky bowel syndrome, ulcers, gastritis, allergic disorders, diverticulitis ...'. ^{126,127}	The product is not generally recognized as safe and effective (GRASE) for the referenced conditions and therefore, the product is a 'new drug'. New drugs may not be legally marketed in the United States without prior approval from FDA.
'Cat's Claw appears to provide cystic action, thus preventing the development and growth of malignant cells in cancer and other tumorous conditions. It helps the immune system, including Aids [sic]. by increasing the production of leukocytes (white blood cells), and blocking the advance of many viral illnesses. Its anti-inflammatory effects are well known for the treatment of conditions such as arthritis (inflammation of the joint), rheumatism, ... gout, fibromyalgia, and Carpal Tunnel Syndrome (CTS)'. ¹²⁸	The product is not generally recognized as safe and effective (GRASE) for the referenced conditions and therefore, the product is a 'new drug'. New drugs may not be legally marketed in the United States without prior approval from FDA.
'Herbal practitioners around the world have used Uncaria tomentosa to treat a variety of conditions including arthritis, AIDS, allergies, ... ulcers, colitis, irritable bowel syndrome, Crohn's disease, and conditions involving chronic inflammation. It further helps lower blood pressure, reduces inflammation, and prevents the spread of tumours and viral infection'. ¹²⁹	The product is not generally recognized as safe and effective (GRASE) for the referenced conditions and therefore, the product is a 'new drug'. New drugs may not be legally marketed in the United States without prior approval from FDA.

¹²⁴ D.D. Tolen, FDA Warning Letter issued to Biogenetics Food Corporation (22 July 1997). Available at: <http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/1997/UCM065731.pdf>.

¹²⁵ D.D. Tolen, FDA Warning Letter issued to Body Systems Technology (15 September 1998). Available at: <http://www.fda.gov/downloads/ICECI/EnforcementActions/WarningLetters/1998/UCM066777.pdf>.

¹²⁶ M. Woleske, FDA Warning Letter issued to Fem Health / Superb Herbs (02 June 2008). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2008/ucm1048261.htm>.

¹²⁷ M. Woleske, FDA Warning Letter issued to New Sun Inc. (09 June 2008). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2008/ucm1048246.htm>.

¹²⁸ H.T. Thornburg, FDA Warning Letter issued to Road to Healing (29 May 2008). Available at: <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2008/ucm1048269.htm>.

¹²⁹ S.J. Walker, FDA Warning Letter issued to Smartbomb Inc. (14 June 2005). Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/CyberLetters/ucm059142.pdf>.

5.8. Yacón

Yacón (*Smallanthus sonchifolia* (Poepp. et Endl.) H. Robinson; Fam. Asteraceae) is not listed in the American Herbal Products Association's (AHPA) *Herbs of Commerce*,¹³⁰ which 'might' be an indication that it was not in United States commerce prior to 15 October 1994. While this suggests that certain processed forms of yacón (leaf or root) might be a New Dietary Ingredient (NDI) if used as a component of a dietary supplement product (DSP), yacón is already marketed as a component of food products (e.g. syrup) and DSPs (usually as a component of a complex mixture in a capsule or tablet). It is also possible that the extract of the leaves is found as a skin conditioning component of non-drug cosmetic products.

Regarding yacón dietary supplement products (DSP) exported by Peruvian companies, there have been some import refusals because FDA determined that the manufacturer's of the yacón products failed to obtain a food canning establishment (FCE) registration, which is a requirement for acidified foods and/or low-acid packaged food products. One import refusal listed two violations for a 'yacón natural extract' product: (1) Misbranded: The article appears to be misbranded in that the label or labelling bears an unauthorized nutrient content/health claim;¹³¹ and (2) Adulteration: It appears that the manufacturer has not filed information on its scheduled process (conditions for heat processing and control of pH, salt, sugar, and preservative levels) as required by 21 CFR 108.25(c)(2)¹³² or 108.35(c)(2).¹³³ Another similar import refusal involved a product described as 'yacón fruit jam' with two violations: (1) Need FCE: It appears the manufacturer is not registered as a low acid canned food or acidified food manufacturer pursuant to 21 CFR 108.25(c)(1) or 108.35(c)(1); and (2) Adulteration: It appears that the manufacturer has not filed information on its scheduled process as required by 21 CFR 108.25(c)(2) or 108.35(c)(2).¹³⁴ The product refused entry, in part, for unauthorized nutrient content claims and unauthorized health claims may have been labelled as it is in Peru with label claims like 'great source of antioxidants' (an unauthorized nutrient content claim for the United States market) and 'keeps your arteries free of cholesterol and triglycerides' (an unauthorized health claim for the United States market).

For the use of yacón as a component of a dietary supplement product that will carry a structure/function claim statement on the product label, no later than 30 days after the first marketing of the product, the manufacturer, packer, or distributor must submit a Notification Letter to FDA (a signed original and two copies) which includes the text of the structure/function statement among other required information. The notice must be signed by the company's responsible person who can certify the accuracy of the information presented and contained in the notice and also certify that the notifying firm has substantiation that the statement is truthful and not misleading.¹³⁵

FDA does not 'approve' claim statements. However, if FDA objects to a claim statement the agency may send a Letter of Objection in response to the Notification Letter. Or through post-marketing surveillance (of product labels and websites) FDA may issue a Warning Letter if they determine that violative claim statements are being made. Warning Letters require immediate action.

Table 13 provides specific examples of notified claim statements for yacón products that FDA has not objected to, as well as violative claim statements that FDA has objected to. Reasons for the acceptability or non-acceptability of each example are provided.

¹³⁰ M. McGuffin, J.T. Kartesz, A.Y. Leung, A.O. Tucker (eds.), *American Herbal Products Association's Herbs of Commerce*, 2nd edition (Silver Spring, Maryland, American Herbal Products Association, 2000).

¹³¹ Food and Drug Administration. Import Refusal Report, Refusal Details as Recorded in OASIS by FDA for Refusal 906-0818082-5/2/1 (27 February 2008). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=906-0818082-5&DocId=2&LineId=1&SfxId=

¹³² Food and Drug Administration, 'Acidified foods', *Code of Federal Regulations*, 21CFR §108.25 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec108-25.pdf>.

¹³³ *Ibid.*, 21CFR §108.35. Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec108-35.pdf>.

¹³⁴ Food and Drug Administration, Import Refusal Report, Refusal Details as Recorded in OASIS by FDA for Refusal AWB-0001465-8/1/1/A (11 March 2004). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=AWB-0001465-8&DocId=1&LineId=1&SfxId=A.

¹³⁵ Food and Drug Administration, 'Certain types of statements for dietary supplements' *Code of Federal Regulations*, 21CFR §101.93 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

Table 13 Acceptable and non-acceptable claim statements for yacón DSPs

Acceptable claim statements	
Claim statement(s)	Reason it is acceptable
Glucose management system. ¹³⁶ Supports glucose metabolism and assists in weight management. ¹³⁷	A general statement that a dietary supplement provides nutritional support can be an acceptable structure/function claim, provided that the statement does not suggest that the supplement is intended to augment or have the same purpose as a specific drug (e.g. insulin), drug action, or therapy for a disease (e.g. diabetes). For example, 'use as part of your diet to help maintain a healthy blood sugar level' would be considered acceptable. Another acceptable structure/function claim would be 'use as a part of your weight loss plan'. ¹³⁸
Non-acceptable claim statements	
Violative claim statement(s)	Reason it is non-acceptable
Great source of antioxidants. ¹³⁹	This would be an unauthorized nutrient content claim. Nutrient content claims using the term 'antioxidant' must also comply with the requirements listed in 21CFR §101.54(g). ¹⁴⁰ These requirements state, in part, that for a product to bear such a claim, a Recommended Daily Intake (RDI) must have been established for each of the nutrients that are the subject of the claim. No RDI has been established by FDA for purple corn extract. Presently beta-carotene, Vitamin C and Vitamin E are the only substances authorized for antioxidant claim statements.
Keeps your arteries free of cholesterol and triglycerides.	References to lowering cholesterol are implied disease claims (hypercholesterolemia). FDA has concluded however that an appropriate and acceptable structure/function claim for maintaining cholesterol would be 'helps to maintain cholesterol levels that are already within the normal range'. ¹⁴¹
Yacón safeguards against colon cancer.	This is a disease claim and/or an unauthorized qualified health claim. For example, a qualified health claim for calcium and colon cancer is permitted as follows: 'Some evidence suggests that calcium supplements may reduce the risk of colon/rectal cancer, however, FDA has determined that this evidence is limited and not conclusive'. ¹⁴²

¹³⁶ J. Morley, FDA Notification Letter for WellBetXTM Glucose Balance Herbal Formula (30 June 2004). Available at: <http://www.fda.gov/ohrms/dockets/dailys/04/aug04/080904/97s-0162-let14210-vol123.pdf>.

¹³⁷ J. Huber, FDA Notification Letter for Optio GlucoFit™ (22 July 2002). Available at: <http://www.fda.gov/ohrms/dockets/dailys/03/Aug03/082503/97s-0162-let10639-vol80.pdf>.

¹³⁸ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register*. Vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

¹³⁹ Food and Drug Administration, Import Refusal Report, Refusal Details as Recorded in OASIS by FDA for Refusal 906-0818082-5/2/1, (27 February 2008). Available at: http://www.accessdata.fda.gov/scripts/importrefusals/ir_detail.cfm?EntryId=906-0818082-5&DocId=2&LineId=1&SfxId=

¹⁴⁰ Food and Drug Administration, 'Nutrient content claims for 'good source', 'high', 'more', and 'high potency', *Code of Federal Regulations*, 21CFR§101.54 (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-54.pdf>.

¹⁴¹ Food and Drug Administration, '21CFR Part 101. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, Final Rule', *Federal Register* vol. 65, No. 4 (6 January 2000). pp. 1000-1050. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2000-01-06/pdf/00-53.pdf>.

¹⁴² Food and Drug Administration, 'Appendix D: Qualified Health Claims', *Guidance for Industry: A Food Labeling Guide* (October 2009). Available at:

6. Example of FDA dietary supplement notification letter

No later than 30 days after the first marketing of a dietary supplement product (DSP), the manufacturer, packer, or distributor must submit a Notification Letter to FDA (a signed original and two copies) which includes the text of the structure/function statement among other required information. The notice must be signed by the company's responsible person who can certify the accuracy of the information presented and contained in the notice and also certify that the notifying firm has substantiation that the statement is truthful and not misleading.¹⁴³ Here follows is an 'example' of a complete FDA Notification Letter including reference to the sections of the regulation for each component of the letter.

Date

Office of Nutritional Products, Labeling and Dietary Supplements (HFS-810)
Center for Food Safety and Applied Nutrition (CFSAN)
Food and Drug Administration (FDA)
5100 Paint Branch Pkwy.
College Park, MD 20740

To whom it may concern,

Pursuant to 21 CFR 101.93 (a) (2), Laboratorios XYZ, [Street Address, City, State, Zip Code] hereby notifies the FDA that it is making the following statements covered by the referenced regulation for its; **Cat's Claw** Herbal Dietary Supplement, containing, per serving XXX mg of organic cat's claw stem bark: '*to support healthy immune function and overall well-being*'.

21 CFR §101.93(a)(2)(i): Name and address of the manufacturer of the dietary supplement that bears the statement:

Laboratorios XYZ, [Street Address, City, State, Zip Code]

21 CFR §101.93(a)(2)(ii): Text of the statements that are being made:

Cat's Claw is used to support healthy immune function and overall well-being.*

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.**

Directions for use: Take XXX capsules XXX times daily.

Cautions and Warnings: Consult a health care practitioner prior to use if you are suffering from autoimmune disorder, blood clotting disorder, and hypotension. If you are taking anticoagulants, immunosuppressant, or antihypertensive agents.

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Centre right away.

21 CFR §101.93(a)(2)(iii): Names of the dietary ingredients that are the subject of the statement:

Organic cat's claw (*Uncaria tomentosa*) inner stem bark XXX mg

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm247933.htm>.

¹⁴³ Food and Drug Administration, 'Certain types of statements for dietary supplements', *Code of Federal Regulations*, 21CFR §101.93, (Washington, DC, United States Government Printing Office, 1 April 2011). Available at: <http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol2/pdf/CFR-2011-title21-vol2-sec101-93.pdf>.

21 CFR §101.93(a)(2)(iv): Name of the dietary supplement (including brand name):

Laboratorios XYZ *Cat's Claw* Herbal Dietary Supplement

21 CFR §101.93(a)(3): Notice signed by a responsible individual who can certify the accuracy of the information presented and contained in the notice:

The undersigned certifies that the information contained in this notice is complete and accurate and that Laboratorios XYZ has substantiation that the statement is truthful and not misleading.

Yours truly,

Name of Responsible Person (printed and signature)

Title of Responsible Person

Laboratorios XYZ

Street Address

City, State

Zip Code



Street address
International Trade Centre
54-56 Rue de Montbrillant
1202 Geneva, Switzerland

P: +41 22 730 0111
F: +41 22 733 4439
E: itcreg@intracen.org
www.intracen.org

Postal address
International Trade Centre
Palais des Nations
1211 Geneva 10, Switzerland

The International Trade Centre (ITC) is the joint agency of the World Trade Organization and the United Nations.