

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2007N-0464]

Health Claims and Qualified Health Claims; Dietary Lipids and Cancer, Soy Protein and Coronary Heart Disease, Antioxidant Vitamins and Certain Cancers, and Selenium and Certain Cancers; Reevaluation; Opportunity for Public Comment

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on its intent to reevaluate the scientific evidence for two previously authorized health claims (dietary lipids (fat) and cancer; soy protein and risk of coronary heart disease) and two qualified health claims that were the subject of letters of enforcement discretion (antioxidant vitamins and risk of certain cancers; selenium and certain cancers). The agency is undertaking a reevaluation of the scientific basis for these authorized health claims and qualified health claims because of new scientific evidence that has emerged for these substance-disease relationships. The new scientific evidence may have the effect of weakening the substance-disease relationship for these authorized health claims and either strengthening or weakening the scientific support for the substance-disease relationship for these qualified health claims.

DATES: Submit written or electronic comments by [*insert date 60 days after date of publication in the Federal Register*].

ADDRESSES: You may submit comments, identified by Docket No. 2007N–0464, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.
- Agency Web site: <http://www.fda.gov/dockets/ecomments>. Follow the instructions for submitting comments on the agency Web site.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301–827–6870.
- Mail/Hand delivery/Courier (for paper, disk, or CD–ROM submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal or the agency Web site, as described previously, in the **ADDRESSES** portion of this document under *Electronic Submissions*.

Instructions: All submissions received must include the agency name and docket number for this notice. All comments received may be posted without change to <http://www.fda.gov/ohrms/dockets/default.htm>, including any personal information provided. For additional information on submitting comments, see the “How to Submit Comments” heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to <http://www.fda.gov/ohrms/dockets/default.htm> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Claudine Kavanaugh, Center for Food Safety and Applied Nutrition (HFS–830), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740–3835, 301–436–1450, FAX: 301–436–2636.

SUPPLEMENTARY INFORMATION:

I. Background

The Nutrition Labeling and Education Act of 1990 (NLEA) (Public Law 101–553) was designed to give consumers more scientifically valid information about foods they eat. Among other provisions, the NLEA directed FDA to issue regulations providing for the use of statements that describe the relationship between a substance and a disease (health claims) in the labeling of foods, including dietary supplements, after such statements have been reviewed and authorized by FDA.¹ For these health claims, that is, statements about substance-disease relationships, FDA has defined the term “substance” by regulation as a specific food or food component (§ 101.14(a)(2) (21 CFR 101.14(a)(2))). An authorized health claim may be used on both conventional foods and dietary supplements, provided that the substance in the product and the product itself meet the appropriate standards in the authorizing regulation. Health claims are directed to the general population or designated subgroups

¹In 1997, Congress enacted the Food and Drug Administration Modernization Act, which established an alternative authorization procedure for health claims based on authoritative statements of certain federal scientific bodies or the National Academy of Sciences. This notice does not address that alternative procedure.

(e.g., the elderly) and are intended to assist the consumer in maintaining healthful dietary practices.

Under section 403(r)(4)(A)(i) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 343(r)(4)(A)(i)), any person may petition FDA to issue a health claim regulation. In evaluating the petition, FDA considers whether there is “significant scientific agreement” (SSA) based on the totality of publicly available scientific evidence concerning the relationship that is the subject of the claim. This standard derives from section 403(r)(3)(B)(i) of the act (21 U.S.C. 343(r)(3)(B)(i)), which provides that FDA shall authorize a health claim to be used on conventional foods if the agency “determines based on the totality of the publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence.” This scientific standard was prescribed by statute for conventional food health claims; by regulation, FDA adopted the same standard for dietary supplements health claims (see § 101.14(c)).

In evaluating a petition for an authorized health claim, if FDA concludes that the evidence supporting the relationship that is the subject of the claim does not meet the SSA standard, the agency considers whether there is credible evidence to support a qualified health claim. FDA may issue a letter of enforcement discretion for a qualified health claim where the totality of scientific evidence supporting the relationship that is the subject of the claim is credible but does not meet the SSA standard. Qualified health claims contain

qualifying language about the level of scientific evidence to ensure consumers receive accurate information about the claim.

The genesis of qualified health claims was the court of appeals decision in *Pearson v. Shalala* (Pearson). In that case, the plaintiffs challenged FDA's decision not to authorize health claims for four specific substance-disease relationships in the labeling of dietary supplements. Although the district court ruled for FDA (14 F. Supp. 2d 10 (D.D.C. 1998)), the U.S. Court of Appeals for the D.C. Circuit reversed the lower court's decision (164 F.3d 650 (D.C. Cir.1999)). The appeals court held that the First Amendment does not permit FDA to reject health claims that the agency determines to be potentially misleading unless the agency also reasonably determines that a disclaimer would not eliminate the potential deception.

In the **Federal Register** of October 26, 1999 (64 FR 57700), the agency authorized a health claim for soy protein and risk of coronary heart disease (21 CFR 101.82). Since authorizing this health claim, numerous studies have evaluated the relationship between soy protein and coronary heart disease, and the findings of these studies are inconsistent. The Agency for Healthcare Research and Quality (AHRQ) released a report in July 2005 outlining the effects of soy products on health outcomes including cardiovascular disease and concluded that soy products appear to exert a small benefit on low-density lipoprotein (LDL)-cholesterol (Ref. 1). However, it is not clear whether soy protein (versus other types of soy products) was responsible for such a benefit. The AHRQ report included studies that evaluated substances in addition to soy protein (e.g., isoflavones). In addition, the AHRQ report used markers of cardiac function (e.g., triglycerides, endothelial function, oxidized LDL) that are not validated surrogate endpoints recognized by the agency for heart

disease risk. The agency intends to evaluate the scientific evidence on soy protein and the risk of coronary heart disease to determine if the totality of the scientific evidence continues to meet the significant scientific agreement standard.

In the **Federal Register** of January 6, 1993 (58 FR 2787), FDA authorized a health claim on dietary lipids (fat) and cancer (21 CFR 101.73). In the years since authorizing this health claim, numerous studies have been published evaluating this substance-disease relationship. The Institute of Medicine (IOM) of the National Academy of Sciences, an authoritative body, published a report that reviewed the evidence on dietary lipid consumption and cancer risk (Ref. 2). The IOM reported in its review of the literature that the association between diets high in fat and increased cancer risk has been weakened by recent epidemiological studies. The IOM report set an acceptable macronutrient distribution range (AMDR) for total fat, however, it was not set based on cancer as a disease outcome because of insufficient scientific evidence linking consumption of fat with cancer risk. One factor in determining the AMDR is the long-term intake level of a nutrient that can minimize the potential for chronic disease. The agency intends to reevaluate the scientific evidence on dietary lipids and cancer risk and determine if the totality of the evidence continues to meet the significant scientific agreement standard.

Section 10.25(b) (21 CFR 10.25(b)) states that the Commissioner of Food and Drugs may initiate a proceeding to issue, amend, or revoke a regulation or take or refrain from taking any other form of administrative action. FDA intends to evaluate whether the currently available scientific evidence concerning the substance-disease relationship for the authorized health claims, dietary lipids and cancer and soy protein and coronary heart disease, continues

to support its previous decisions on these authorized health claims. If the agency decides to take action to amend or revoke one or both of these health claims, after completing its review of the current scientific evidence, the agency will publish its findings and solicit comments on them before the agency takes any action with respect to revising the particular health claim. Interested persons may submit scientific information about these two specific health claims in response to this notice.

In 2003, FDA issued two letters on the use of the agency's enforcement discretion for qualified health claims on antioxidant vitamins (vitamins E and C) and risk of certain cancers (Ref. 3) and selenium and certain cancers and anticarcinogenic effects in the body (Ref. 4). In May 2006, AHRQ issued a report evaluating the use of multivitamin/mineral supplements and the risk of chronic disease (Ref. 5). The report did not identify any studies on the efficacy of vitamin C supplements and cancer risk. In addition, the report concluded that the overall strength of the evidence for vitamin E and selenium supplements on cancer risk is very low (vitamin E) and low (selenium). The agency intends to reevaluate the scientific evidence on these two qualified health claims and determine if the scientific evidence continues to support the qualified health claim, and if so, whether the qualified health claim language should be modified to reflect a stronger or weaker relationship.

If the agency decides a change may be needed with respect to one or both of these claims, the agency intends to publish its findings and solicit comments on them. Interested persons may submit scientific information about these two specific qualified health claims in response to this notice.

Reevaluating Cancer Health Claims by Cancer Site

In the final rule authorizing a health claim for dietary fat and cancer, FDA considered whether such a claim should specifically address the types of cancer affected by a diet that is low in total fat, or whether the claim should not be site-specific (58 FR 2787 at 2788 through 2789). FDA ultimately decided that the identification of specific sites of affected cancers would not be appropriate due, in part, to weaker data on the relationship between dietary fat and breast cancer and the possibility of a wider variety of affected sites for the dietary fat and cancer relationship. Therefore, FDA required that the terms “some types of cancer” or “some cancers” be used in specifying the disease for this health claim relationship (*id.*). The antioxidant and cancer and selenium and cancer qualified health claims also contain similar language, *i.e.*, “certain forms of cancer,” to be used in specifying the disease. However, in other qualified health claims for a substance and cancer relationship (Refs. 6, 7, and 8), the agency considered separate qualified health claims for each type of cancer.

Cancer is a constellation of more than 100 different diseases, each characterized by the uncontrolled growth and spread of abnormal cells (Ref. 9). Cancer is categorized into different types of diseases based on the organ and tissue sites (Ref. 10). Cancers at different organ sites have different risk factors, treatment modalities, and mortality risk (Ref. 9). Both genetic and environmental (including diet) risk factors may affect the risk of different types of cancers. Risk factors may include a family history of a specific type of cancer, cigarette smoking, alcohol consumption, overweight and obesity, exposure to ultraviolet or ionizing radiation, exposure to cancer-causing chemicals, and dietary factors. The etiology, risk factors, diagnosis, and

treatment for each type of cancer are unique (Refs. 11 and 12). Because each form of cancer is a unique disease based on organ site, risk factors, treatment options, and mortality risk, FDA's current approach is to evaluate each form of cancer individually in a health claim or qualified health claim petition to determine whether the scientific evidence supports the potential substance-disease relationship for any type of cancer, each of which constitutes a disease under § 101.14(a)(5).

The agency intends to consider, as part of its reevaluation of the scientific evidence for dietary fat, antioxidant, and selenium and their association with a reduced risk of cancer, claim language to reflect specific types of cancer rather than "certain forms of cancer" (or similar language).

II. How to Submit Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individual may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Please note that in January 2008, the FDA Web site is expected to transition to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. After the transition date, electronic submissions will be accepted by FDA through the FDMS only. When the exact date of the transition to FDMS is known, FDA will publish a **Federal Register** notice announcing that date.

III. References

The following references have been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site addresses, but we are not responsible for subsequent changes to the Web sites after this document publishes in the **Federal Register**.)

1. Balk E, Chung M, Chew P, Ip S, Raman G, Kupelnick B, Tatsioni A, Sun Y, Wolk B, DeVine D, Lau J. Effects of Soy on Health Outcomes. Summary, Evidence Report/Technology Assessment No. 126. (Prepared by the Tufts-New England Medical Center Evidence-based Practice Center under Contract No. 290-02-0022.) AHRQ Publication No. 05-E024-1. Rockville, MD: Agency for Healthcare Research and Quality. July 2005.

2. Institute of Medicine, National Academy of Sciences. *Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids, Chapter 11 page 808*. National Academy Press. Washington, D.C. 2005.

3. Antioxidant vitamins and risk of certain cancers, April 1, 2003, <http://www.cfsan.fda.gov/~dms/ds-ltr34.html>.

4. Selenium and certain cancers, February 21, 2003, Docket No. 2002P-0457 (formerly Docket No. 02P-0457), <http://www.cfsan.fda.gov/~dms/ds-ltr35.html>.

5. Huang HY, Caballero B, Chang S, Alberg A, Semba R, Schneyer C, Wilson RF, Cheng TY, Prokopowicz G, Barnes II GJ, Vassy J, Bass EB. Multivitamin/Mineral Supplements and Prevention of Chronic Disease. Evidence Report/Technology Assessment No. 139. (Prepared by The Johns Hopkins University Evidence-based Practice Center under Contract No. 290-02-0018). AHRQ Publication No. 06-E012. Rockville, MD: Agency for Healthcare Research and Quality. May 2006.

6. Tomatoes and prostate, ovarian, gastric and pancreatic cancers, November 8, 2005, Docket No. 2004Q-0201, <http://www.cfsan.fda.gov/~dms/qhclyco.html>.
7. Green tea and prostate and breast cancer risk, June 30, 2005, Docket No. 2004Q-0083, <http://www.cfsan.fda.gov/~dms/qhc-gtea.html>.
8. Calcium and colon/rectal, breast and prostate cancers and recurrent polyps, October 12, 2005, Docket No. 2004Q-0097, <http://www.cfsan.fda.gov/~dms/qhcca2.html>.
9. American Cancer Society, Cancer Facts and Figures, 2004.
10. National Cancer Institute, Dictionary of Cancer Terms, http://www.cancer.gov/Templates/db_alpha.aspx?CdrID=45333.
11. Hord NG, Fenton JI. Context is everything: mining the normal and preneoplastic microenvironment for insights into the diet and cancer risk conundrum. *Molecular Nutrition and Food Research*, 2007, 51:100–106.
12. Milner JA. Diet and Cancer: Facts and Controversies. *Nutrition and Cancer*, 2006, 56:216–224.

Dated: December 6, 2007.

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