

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket No. 98N-0426]

Food Labeling: Health Claims; Antioxidant Vitamins C and E and the Risk in Adults of Atherosclerosis, Coronary Heart Disease, Certain Cancers, and Cataracts

AGENCY: Food and Drug Administration, HHS.

ACTION: Interim final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing an interim final rule to prohibit the use on foods of a claim relating to the relationship between antioxidant vitamins C and E and the risk in adults of atherosclerosis, coronary heart disease, certain cancers, and cataracts. This rule is in response to a notification of a health claim submitted under section 303 of the FDA Modernization Act of 1997 (FDAMA). FDA has reviewed statements that the petitioner submitted in that notification, and, in conformity with the requirements of FDAMA, the agency is prohibiting the claim because the statements submitted as the basis of the claim are not "authoritative statements" of a scientific body, as required by FDAMA; therefore, section 303 of FDAMA does not authorize use of this claim. As provided for in section 301 of FDAMA, this rule is effective immediately upon publication.

DATES: The interim final rule is effective June 22, 1998; comments by September 8, 1998.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Christine J. Lewis, Center for Food Safety and Applied Nutrition (HFS-451), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-205-4168.

SUPPLEMENTARY INFORMATION:

I. The FDA Modernization Act of 1997

On November 21, 1997, the President signed FDAMA into law (Pub. L. 105-115), which amended the Federal Food, Drug, and Cosmetic Act (the act). Sections 303 and 304 of FDAMA amended section 403(r)(2) and (r)(3) of the act by adding new paragraphs (r)(2)(G), (r)(2)(H), (r)(3)(C), and (r)(3)(D)

to section 403 of the act (21 U.S.C. 343(r)(2)(G), (r)(2)(H), (r)(3)(C), and (r)(3)(D), respectively), which provide for the use in food labeling of nutrient content claims and health claims, respectively, based on authoritative statements. These provisions of FDAMA supplement the petition process for nutrient content and health claims provided by section 403(r)(4) (21 U.S.C. 343(r)(4)) and §§ 101.69 and 101.70 (21 CFR 101.69 and 101.70, respectively) by providing an alternative for establishing the scientific basis for such claims by reliance on authoritative statements.

FDAMA requires that a notification of the prospective nutrient content claim or the prospective health claim be submitted to FDA at least 120 days before a food bearing the claim may be introduced into interstate commerce. The notification must contain specific information including: (1) The exact wording of the prospective nutrient content claim or health claim; (2) a concise description of the basis upon which the petitioner relied for determining that the requirements of section 403(r)(2)(G)(i) of the act for nutrient content claims or section 403(r)(3)(C)(i) for health claims have been satisfied; (3) a copy of the authoritative statement that serves as the basis for the claim; and (4) a balanced representation of the scientific literature relating to the nutrient level for a prospective nutrient content claim or relating to the relationship between the nutrient and the disease or health-related condition for a prospective health claim. For a prospective nutrient content claim, the authoritative statement must identify the nutrient level to which the claim refers. For a prospective health claim, the authoritative statement must be a statement about the relationship between a nutrient and a disease or health-related condition to which the claim refers. For both types of claims, the authoritative statement must be currently in effect and it must have been published either by a scientific body of the U.S. Government that has official responsibility for public health protection or research directly relating to human nutrition (e.g., the National Institutes of Health (NIH) or the Centers for Disease Control and Prevention (CDC)) or by the National Academy of Sciences (NAS) or any of its subdivisions (hereinafter referred to as a "scientific body").

Under new section 403(r)(2)(H) and (r)(3)(D) of the act, such a claim may be made beginning 120 days after submission of the notification until: (1) FDA has issued an effective regulation that prohibits or modifies the claim; (2)

the agency has issued a regulation finding that the requirements under section 403(r)(2)(G) for a prospective nutrient content claim or under section 403(r)(3)(C) for a prospective health claim have not been met; or (3) a district court of the United States in an enforcement proceeding under chapter III of the act has determined that the requirements under section 403(r)(2)(G) for a prospective nutrient content claim or under section 403(r)(3)(C) for a prospective health claim have not been met. During the 120 days following submission of a notification and before the claim may appear on a food, the agency may also notify any person who is making the claim that the notification did not include all of the required information.

Section 304 of FDAMA permits nutrient content claims based on authoritative statements for both conventional foods and for dietary supplements because section 304 amended section 403(r)(2) of the act, which provides for nutrient content claims on both conventional foods and dietary supplements. Section 303 of FDAMA does not include provisions for health claims for dietary supplements based on authoritative statements, however. In particular, section 403(r)(5)(D) of the act (21 U.S.C. 343(r)(5)(D)) specifies that health claims for dietary supplements shall not be subject to section 403(r)(3) of the act, but rather to a procedure and standard that FDA establishes by regulation. In section 303 of FDAMA, Congress amended section 403(r)(3) of the act, which provides for procedures and standards for health claims for conventional foods, to allow for health claims based on authoritative statements for conventional foods, but Congress did not amend section 403(r)(5)(D) of the act.

Therefore, FDA believes that section 403(r)(3)(C) of the act authorizes use of a health claim based on an authoritative statement only on any conventional food that provides an appropriate level of the nutrient that is the subject of the health claim, that does not exceed the disqualifying levels identified in § 101.14(a)(5) (21 CFR 101.14(a)(5)), and that otherwise complies with section 403(r)(3)(C) and all other provisions of the act. Nevertheless, FDA has tentatively concluded that, for health claims authorized via the authoritative statement procedure provided by FDAMA, conventional foods and dietary supplements should be subject to the same standards and procedures. This position is consistent with the agency's final rule that made dietary supplements subject to the same general

requirements as apply to conventional foods with respect to health claims (59 FR 395, January 4, 1994). This approach is also consistent with the guidance of the Commission on Dietary Supplement Labels, which stated in its 1997 report (Ref. 1) that the process for the approval of health claims should remain the same for dietary supplements and conventional foods. Therefore, FDA intends to issue a proposed rule to provide for health claims based on authoritative statements for dietary supplements.

A. Authoritative Statements

Sections 303 and 304 of FDAMA authorize the use of a health or nutrient content claim based, in part, on an "authoritative statement." In particular, new section 403(r)(3)(C)(i) and (r)(2)(G)(i) of the act states that such claims are authorized and may be made when "a scientific body * * * has published an authoritative statement, which is currently in effect." For a health claim, section 403(r)(3)(C)(i) of the act requires that the statement must be "about the relationship between a nutrient and a disease or health-related condition to which the claim refers." For a nutrient content claim, section 403(r)(2)(G)(i) of the act requires that the statement must be one "that identifies the nutrient level to which the claim refers."

Section 403(r)(3)(C) and (r)(2)(G) of the act further requires that:

* * * [a] statement shall be regarded as an authoritative statement of a scientific body described in subclause (i) only if the statement is published by the scientific body and shall not include the statement of an employee of the scientific body made in the individual capacity of the employee.

Although Congress did not explicitly define the term "authoritative statement," section 403(r)(3)(C) and (r)(2)(G) of the act and the legislative history clarify several characteristics that Congress intended an "authoritative statement" to have. Most significantly, to be the basis for a health or nutrient content claim, a statement must: (1) Address certain subjects, namely, for a health claim, it must be about the relationship between a nutrient and a disease or health-related condition to which the claim refers, or, for a nutrient content claim, it must identify the nutrient level to which the claim refers; (2) be published by an appropriate scientific body and represent its official position, and may not be, for example, a statement of individual employees of the scientific body made in the individual capacities of the employees; (3) be based on a deliberative review of the scientific evidence on the subject of

the statement and not indicate that the scientific evidence about the subject of the statement is preliminary or inconclusive; and (4) be currently in effect. The aspects of these requirements relevant to this rulemaking, and its companion rulemakings publishing elsewhere in this issue of the **Federal Register**, are discussed in greater detail in section I.A.1 of this document.

1. To Be the Basis for a Health or Nutrient Content Claim, a Statement Must Address One of Two Subjects

For a statement to be eligible for consideration as an "authoritative statement," it must address certain subjects. Section 403(r)(3)(C) of the act provides that, for a health claim, it must be "about the relationship between a nutrient and a disease or health-related condition to which the claim refers." Section 403(r)(2)(G) of the act provides that, for a nutrient content claim, it must "identify the nutrient level to which the claim refers."

There are several aspects to these requirements. First, a statement cannot be an "authoritative statement" under section 403(r)(2)(G) or (r)(3)(C) of the act if it identifies no nutrient level or if it is not about the relationship between a nutrient and a disease or health-related condition. For example, if a statement refers to no nutrient, to no disease or health-related condition, or to neither a nutrient nor a disease or health-related condition, it cannot be an authoritative statement under section 403(r)(3)(C) of the act. Second, if a statement is "about the relationship between a nutrient and a disease or health-related condition," or if it "identif[ies] the nutrient level," it must be about the relationship or nutrient "to which the claim refers." Moreover, the statement must be about the relationship between a nutrient and a disease or health-related condition in humans or it must identify a nutrient level for total daily consumption by humans.

When evaluating what relationship a statement is about, or what nutrient level a statement identifies, it may be necessary to consider the context in which the statement appears. It is likely that a submitter will identify excerpted sentences as an "authoritative statement." The context in which these excerpted sentences appears can be relevant when determining the subject of the statement. For example, sentences immediately adjoining the excerpted sentences or in a summary statement in the document may clarify the disease that is the subject of the excerpted sentences.

Accordingly, the statutory requirement in section 403(r)(3)(C)(ii)(II)

and (r)(2)(G)(ii)(II) of the act that a notification include "a copy of the statement referred to in subclause (i) upon which [the] person [who submitted the notification] relied in making the claim," means that the entire document from which the statement is excerpted should be included in a notification. The agency notes that submission of the entire document is also relevant to other determinations under section 403(r)(3)(C) and (r)(2)(G), such as whether the scientific evidence about the relationship or nutrient level at issue is preliminary or inconclusive, as discussed in section I.A.3 of this document, and whether a health or nutrient content claim is "stated in a manner so that the claim is an accurate representation of the authoritative statement referred to in subclause (i)," as required by section 403(r)(3)(C)(iv) and (r)(2)(G)(iv) of the act.

2. To Be the Basis for a Health or Nutrient Content Claim, a Statement Must Be Published by an Appropriate Scientific Body and Represent the Official Policy of That Body.

Section 403(r)(3)(C) and (r)(2)(G) of the act requires that an "authoritative statement" be "published." The agency understands the use of "published" in section 403(r)(3)(C)(i) and (r)(2)(G)(i) to mean that the statement must be publicly available in print form (paper or electronic).

The identical last sentence of section 403(r)(3)(C) and (r)(2)(G) of the act states that:

* * * [a] statement shall be regarded as an authoritative statement of a scientific body described in subclause (i) only if the statement is published by the scientific body and shall not include the statement of an employee of the scientific body made in the individual capacity of the employee. "Published" as used in this sentence means that the scientific body can be considered to be the author of the statement, in that the statement represents the official policy of the scientific body. Of course, the statements of scientific bodies—indeed, of organizations generally—are authored by individuals. Yet statements that are merely those of individual employees made in the individual capacities of the employees are not statements that have been authored by, and so represent the official policy of, the scientific body. Similarly, in the case of Federal scientific bodies with subdivisions, such as NIH and CDC, section 403(r)(3)(C) and (r)(2)(G) indicates that the scientific body, and not merely the subdivision, can be considered to have "published" a statement within the

meaning of those sections only if, as the legislative history indicates, "statements issued by entities such as NIH and CDC reflect consensus within those institutions" (H. Conf. Rept. 105-399, at 98 (1997)). Accordingly, to be considered an "authoritative statement" under section 403(r)(3)(C) and (r)(2)(G), a statement must represent the official policy of a scientific body.

3. To Be the Basis for a Health or Nutrient Content Claim, a Statement Must Be Based on a Deliberative Review of the Scientific Evidence on the Subject of the Statement, and It Should Not Indicate That the Scientific Evidence Is Preliminary or Inconclusive

In section 403(r)(3)(C)(i) and (r)(2)(G)(i) of the act, Congress required that claims may be authorized only when "a scientific body * * * has published an *authoritative statement*," not merely when a scientific body has published a statement (emphasis added). The use of "authoritative" here indicates that a statement may not be the basis for a health or nutrient content claim merely because its source is a scientific body, an authority on the subject of the statement. A review of the legislative history of sections 303 and 304 of FDAMA indicates that, to be "authoritative," Congress intended that a statement must be the product of a deliberative review of the scientific evidence on the subject of the statement. In addition, the statement should not indicate that the scientific evidence about the subject of the statement is preliminary or inconclusive.

Congress intended both that claims based on authoritative statements should have "a presumption of validity" (H. Rept. 105-306, at 16 and 17 (1997)) and that "more *scientifically sound* nutrition information * * * be provided to consumers through health and nutrient content claims" based on authoritative statements (H. Conf. Rept. 105-399, at 98 (1997) (emphasis added); see also H. Rept. 105-306, at 16 (1997) and S. Rept. 105-43, at 49 (1997)).

When FDA authorizes a health claim by regulation under section 403(r)(3)(B) of the act or establishes a Daily Value that can serve as the basis for a nutrient content claim, it conducts a deliberative review of the scientific evidence about the relationship between a nutrient and a disease or health-related condition or about the nutrient level at issue and concludes that there is significant scientific agreement about the relationship or appropriate scientific consensus about the nutrient level. Congress intended that an "authoritative statement" published by a scientific body could be the basis for health and

nutrient content claims because the "authoritative statement" is to serve as a presumptive surrogate for FDA's deliberative review of the scientific evidence.

Congress therefore intended that an "authoritative statement" must be the product of a deliberative review of the scientific evidence on the subject of the statement. For example, the House Report states that:

[a]uthoritative scientific bodies, as part of their official responsibilities for public health protection, regularly undertake deliberative reviews of the scientific evidence to evaluate potential diet/disease relationships, and issue authoritative statements concerning such relationships.

(H. Rept. 105-306, at 16 (1997)). The Senate Report repeats this idea, noting that scientific bodies engage in:

* * * deliberative processes * * * in issuing statements on matters of public health. Important Federal public health organizations, as part of their official responsibilities, routinely review the scientific evidence pertinent to diet and disease relationships, and publish statements developed through such reviews. (S. Rept. 105-43, at 49 (1997)).

Moreover, only a statement that a relationship between a nutrient and a disease or health-related condition exists or that identifies a level of a nutrient—and not merely statements about a possible relationship or level—can serve as the basis for claims that will provide consumers with scientifically sound information. Only a claim based on such a statement can be accorded a presumption of validity.

Accordingly, a statement that indicates, for example, that research about a nutrient level or a relationship between a nutrient and a disease or health-related condition is preliminary or inconclusive, that indicates that such a relationship or a nutrient level is or should be the subject of ongoing scientific study, or that indicates the direction for future research about such a relationship or a nutrient level is not "authoritative." When evaluating whether a statement about a relationship or nutrient level indicates that the scientific evidence is preliminary or inconclusive, the agency intends to consider the context in which the statement appears, as discussed in section I.A.1 of this document. For example, a statement of excerpted sentences might not indicate that research is preliminary or that there are unresolved questions that require additional study, but such qualifiers could be found elsewhere in the document.

The agency notes that, even if a statement meets the criteria to be an "authoritative statement," Congress also

provided under new section 403(r)(3)(D)(i) of the act that FDA have the authority to prohibit a health claim based on an authoritative statement when there is not significant scientific agreement that there is a relationship between the nutrient and the disease or health-related condition in question. As the Senate Report on the provision explains, in an agency rulemaking to prohibit or modify a health claim based on an authoritative statement, "the standards and criteria for health claims prescribed by section 403(r)(3) and implementing regulations, including the significant[t] scientific agreement standard, would be fully applicable" (S. Rept. 105-43, at 51 (1997); see also H. Rept. 105-306, at 15 (1997)).

With respect to nutrient content claims, Congress indicated that the agency is to determine "whether the authoritative statement upon which the notification is based is supported by scientific consensus to the extent * * * appropriate to allow the claim" (H. Rept. 105-306, at 17-18 (1997)), an evaluation that FDA would make under section 403(r)(2)(H) of the act, after the Federal scientific body that is the source of a statement determines that the statement reflects consensus within it, as discussed in section I.A.2 of this document.

B. Review Process

As allowed by sections 303 and 304 of FDAMA, health claims and nutrient content claims based on authoritative statements from Federal scientific bodies or NAS may be made on foods in interstate commerce as soon as 120 days after submission of a notification of the claim to FDA. Upon receipt of a notification, FDA intends to review the notification to determine whether the components specified in section 403(r)(2)(G) and (r)(3)(C) are present within the submission packet. When such components are missing, FDA intends to notify the submitter by letter identifying one or more of these components that is absent from the notification packet.

If the necessary components are present, FDA intends to determine, for a health claim, what relationship between a nutrient and disease or health-related condition is at issue, or, for a nutrient content claim, what nutrient is at issue. If, by regulation under section 403(r)(3)(B) of the act, the agency has already authorized a health claim about the relationship at issue, then the notification provisions of section 403(r)(3)(C) of the act may not be used to modify the existing health claim or to authorize the prospective health claim. Similarly, if by rulemaking the

agency has already established a Daily Value for the nutrient at issue, then the notification provisions of section 403(r)(2)(G) of the act may not be used to modify the existing Daily Value. Instead, a health claim about the relationship at issue or a nutrient content claim referring to the nutrient at issue may be made when the claim is consistent with the existing health claim regulation or with the established Daily Value and the authorized terms for nutrient content claims. Furthermore, if the prospective claim refers to a relationship or a nutrient that is not addressed by the statement that is identified as the "authoritative statement" on which the claim is based, then section 403(r)(3)(C) and (r)(2)(G) of the act does not authorize the health or nutrient content claim at issue. In each case, FDA intends to notify the submitter by letter that use of the claim is not authorized under section 403(r)(3)(C) or (r)(2)(G) of the act, as appropriate.

If, however, a prospective claim could be authorized based on an appropriate authoritative statement, and if the prospective claim refers to a relationship or nutrient that is addressed by the statement that is identified in the notification as the "authoritative statement," FDA then intends to evaluate further whether the statement is an "authoritative statement." In particular, FDA intends to determine for a statement, as a threshold matter, whether: (1) It may be attributable to a scientific body or to one or more of its employees; (2) it is publicly available in print form (paper or electronic); and (3) the statement indicates that the scientific evidence about the relationship between a nutrient and a disease or health-related condition or a nutrient level is preliminary or inconclusive. With respect to the first of these issues, FDA notes that it can determine that a statement from a non-Federal body or agency—such as a state university school of public health—is not an "authoritative statement," or that a statement from a scientist who was not an employee of an appropriate scientific body is not an "authoritative statement." As a general matter, however, only a scientific body can state whether a statement that is attributable to it or to one or more of its employees actually represents the official policy of the scientific body or not, and FDA would therefore consult with the scientific body if necessary.

If a statement fails to meet any of these criteria, FDA would normally conclude that the statement is not an authoritative statement. In any case the

agency may, and, when a statement meets these three criteria, the agency would normally, consult with the scientific body to which the statement is attributed. FDA would request that the scientific body determine, for example, whether the statement is currently in effect; whether the statement represents the official policy of the scientific body, for example, by reflecting consensus within that body, as opposed to being the statement of individual employees made in the individual capacities of those employees; and whether the statement is based on a deliberative review of the scientific evidence.

If the statement is found to be issued by an appropriate scientific body and determined to be an "authoritative statement" under section 403(r)(2)(G) or (r)(3)(C) of the act, the agency intends to review the wording of the claim to determine if it is in accordance with section 403(r)(3)(C)(iv) or (r)(2)(G)(iv) of the act. These provisions of the act require that the claim be stated in a manner so that it is an accurate representation of the authoritative statement and so that the claim enables the public to comprehend the information provided in the claim and to understand the relative significance of such information in the context of a total daily diet.

For health claims, FDA also intends to consider the requirement of section 403(r)(3)(C)(iii) of the act that there be compliance with, for example, sections 403(a) and 201(n) of the act (21 U.S.C. 321(n)), which require that the claim be truthful and not misleading, including compliance as appropriate with existing § 101.14. FDA would also determine whether there is significant scientific agreement concerning the authoritative statement, as provided for under new section 403(r)(3)(D)(i) of the act. For nutrient content claims, FDA intends to consider the requirements of section 403(r)(2)(G)(iii) of the act that there be compliance with, for example, section 403(r)(2)(A)(i) of the act, which requires that nutrient content claims use the terms defined in FDA's regulations, and sections 403(a) and 201(n) of the act, including compliance as appropriate with existing § 101.13 (21 CFR 101.13). If, after this review, FDA has no objections to the claim, then the statute provides that the claim may be used on food labels 120 days after submission of a complete notification.

By contrast, if the statement is not from an appropriate scientific body or is found not to be an "authoritative statement" from a Federal scientific body or NAS (or any of its subdivisions), the agency intends to determine that the notification does not

meet the requirements of section 403(r)(3)(C) or (r)(2)(G) of the act in that the submitter has not submitted a statement from a Federal scientific body or NAS, or an authoritative statement from such a body. The agency may notify the submitter of this determination, and its basis, by letter. Alternatively, the agency may issue an interim final rule to prohibit the claim.

Generally, the agency would notify the submitter by letter when, for example, the notification is deficient on its face, and the agency would use the rulemaking process when substantial scientific or legal questions are presented by the notification. The agency intends to elaborate further on these issues in implementing regulations. The agency has chosen to respond with nine interim rules publishing in this issue of the **Federal Register** to a notification for nine claims to specify the approach used by the agency to review this notification in the absence of implementing regulations, and to provide opportunity for public comment. In the future, the agency anticipates that it may respond to similar notifications by letter. Whether FDA sends a letter or acts by rulemaking to prohibit a claim, the agency may begin an enforcement action under the act in a U. S. district court if such a claim is used in food labeling.

The agency notes that, when it sends such a letter or acts by regulation to prohibit the use of a claim, a person nonetheless may submit in the future a notification that bases the claim on a statement that meets the requirements of section 403(r)(3)(C) or (r)(2)(G) of the act. If there is no authoritative statement that may serve as a basis for the claim, an interested person may petition the agency under section 403(r)(4) of the act and § 101.70 to authorize the health claim by regulation under section 403(r)(3)(B) of the act. For a nutrient content claim, an interested person may submit a citizen petition under 21 CFR 10.30 that requests the agency to establish the Daily Value to which the claim would refer.

II. The Notification

Section 403(r)(2)(G) and (r)(3)(C) of the act became effective on February 19, 1998. On February 23, 1998, the agency received a notification from Weider Nutrition International, Inc., containing nine prospective claims that were identified in the text of the notification as health claims (Ref. 2). The notification included statements that the submitter described as authoritative statements and a scientific literature review for each claim. FDA has created nine separate dockets, one for each of

the nine claims and is issuing a separate interim final rule responding to each claim.

This interim final rule addresses the first claim in the notification. The notification included six statements that the petitioner identified as authoritative statements on which the following claim is based: "Antioxidant vitamins C and E may reduce the risk in adults of atherosclerosis, coronary heart disease, certain cancers, and cataracts. Sources of Vitamin C and E include fruits, vegetables, and dietary supplements."

The first sentence of this claim will be discussed in greater detail in section III of this document. FDA notes that this claim describes the relationship between vitamins C and E and a number of different diseases and, thus, in point of fact, reflects several prospective health claims. The second sentence, "Sources of Vitamin C and E include fruits, vegetables, and dietary supplements," is not a health claim. Given that the notification indicated that it was intended to be a notification for health claims, this statement was not reviewed by FDA. The submitter did not separately identify this statement as any particular type of claim.

Nonetheless, as a point of information, the agency wishes to highlight that statements that appropriately constitute nutrient content claims are allowed on labels and in the labeling of foods and dietary supplements. Moreover, statements that constitute dietary guidance are also allowed provided the information is truthful and not misleading as required by sections 403(a) and 201(n) of the act.

With respect to nutrient content claims, FDA concluded in comment 152 of its final rule for nutrient content claims (58 FR 2302 at 2345, January 6, 1993) that the term "source" alone merely connotes that a nutrient is present and does not provide consumers with meaningful information about the level of the nutrient. Therefore, FDA did not define the term "source," although it did define several other terms that include the word "source." For example, a food is defined as a "good source" of a nutrient if it contains 10 to 19 percent of the Reference Daily Intake (RDI) for that nutrient per reference amount customarily consumed (§ 101.54(c) (21 CFR 101.54(c))), or as an "excellent source" if it contains 20 percent or more of a nutrient's RDI per reference amount customarily consumed (§ 101.54(b)). In addition, "trivial source" is defined as a synonym for "free" and "low source" as a synonym for "low" (see, for example, 21 CFR 101.61(b)(1) and (b)(4)).

Information regarding the agency's position on nutrient content claims is included in the preamble to the proposed and final rules for nutrient content claims (56 FR 60421, November 27, 1991, and 58 FR 2302, January 6, 1993) and in the agency guidance document, "Food Labeling—Questions and Answers—Volume I—For Guidance to Facilitate the Process of Developing or Revising Labels for Foods Other than Dietary Supplements" (Ref. 3).

As for statements that constitute dietary guidance, such label information must be truthful and not misleading as discussed in section II.D.6 of the preamble to the final rule for general requirements for health claims (58 FR 2478 at 2487, January 6, 1993) and in the agency guidance document, "Food Labeling—Questions and Answers—Volume II—A Guide for Restaurants and Other Retail Establishments" (Ref. 4). The agency notes that in the case of the subject sentence, not all fruits, vegetables, and dietary supplements contain significant amounts of vitamins C and E, and therefore if the statement were intended to reflect dietary guidance it cannot be considered to be truthful and not misleading. In addition, to be truthful and not misleading when used on a particular food's labeling, that food must contain significant amounts of vitamins C and E.

III. Basis for the Action

FDA has reviewed the notification submitted in support of the prospective claim: "Antioxidant vitamins C and E may reduce the risk in adults of atherosclerosis, coronary heart disease, certain cancers, and cataracts." The agency has determined that none of the six statements submitted as the basis for this claim meets the requirements in section 403(r)(3)(C) of the act to be an "authoritative statement." Because the prospective claim is not based on an authoritative statement, it is not appropriate for the claim to appear on food labels and labeling. Consequently, FDA is issuing this interim final rule to prohibit the use of this claim. A discussion of the basis for the agency's action on the notification follows.

First, FDA determined that the components required by section 403(r)(3)(C) of the act were present in the notification submitted to support this claim. Second, FDA determined that, as a threshold matter, each of the six statements cited in support of the claim may be attributable either to an appropriate Federal scientific body or to an employee or employees of such a body.

The notification in support of the claim that is the subject of this

document cites statements from: (1) A published article authored by two employees of CDC; (2) public information provided on the Internet by an institute of NIH; (3) an electronic version provided on the Internet of "Nutrition and Your Health: Dietary Guidelines for Americans," (Home and Garden Bulletin No. 232, Fourth Edition, 1995) (hereinafter, referred to as "the dietary guidelines") recommendations developed by a group of Federal agencies and issued jointly by the Department of Health and Human Services (DHHS) and the United States Department of Agriculture (USDA); (4) public information provided on the Internet by CDC's Office of Women's Health; (5) a NIH press release provided on the Internet; and (6) an electronic version provided on the Internet of a quarterly report from USDA's Agricultural Research Service (ARS). Thus, the statements in the notification are attributable to NIH, CDC, and USDA/ARS, as well as a group of Federal agencies that included NIH, CDC, and USDA/ARS. Two of the scientific bodies identified, NIH and CDC, are highlighted in the statute as Federal scientific bodies. FDA believes that USDA/ARS is also a scientific body of the U.S. Government with official responsibility for public health protection or research directly relating to human nutrition for the purposes of section 403(r)(2)(G) and (r)(3)(C) of the act. The group that developed the dietary guidelines included Federal agencies that are such scientific bodies. Accordingly, the statements provided in the notification in support of the claim may be attributable to appropriate Federal scientific bodies or to their employees.

Finally, however, none of the six statements discussed in A. through F. of this section of this document was found to be an authoritative statement.

A. Statement 1

Statement 1 reads: "Antioxidant micronutrients, especially carotenes, vitamin C, and vitamin E, appear to play many important roles in protecting the body against cancer. They block the formation of chemical carcinogens in the stomach, protect DNA and lipid membranes from oxidative damage, and enhance immune function." The notification identified Statement 1 as an "authoritative statement" for purposes of making the claim that is the subject of this rulemaking. The statement is found in the conclusion section of an article published in *The Annual Review of Nutrition* (12:139–59:1992), entitled: "Dietary Carotenes, Vitamin C, and Vitamin E as Protective Antioxidants in

Human Cancers," and authored by two persons, T. Byers and G. Perry, who are identified in the article as employees of CDC at the time of publication of the article. *The Annual Review of Nutrition* is published periodically by Annual Reviews, Inc., in Palo Alto, CA. Editors for each volume serve as reviewers for the various articles included in the volume and contributors are asked to submit articles for consideration for publication. The subject article is 20 pages of a review of the literature that includes a section on the theoretical roles of dietary oxidants in cancer prevention and focuses on the outcomes of laboratory animal research and epidemiologic studies conducted since 1987. The subject statement appears in the conclusion section of the paper. The agency notes that the next sentence in the conclusion section states: "Nevertheless, many important questions need to be answered before either micronutrient supplements or food fortification can be recommended as a cancer prevention strategy to the general population."

The noted qualifying sentence, as well as the wording of the statement itself (i.e., "appear to play"), suggests that the scientific evidence about the relationship in question is preliminary or inconclusive, as discussed in section I.A.3 of this document.

FDA asked CDC whether the statement is an "authoritative statement" under FDAMA. CDC responded to FDA that the statement is not an authoritative statement of CDC because it does not reflect consensus within CDC and was not published by CDC (Ref. 5). CDC indicated that the article was authored by individual employees made in the individual capacity of those employees. Therefore, FDA has concluded that the statement is not an "authoritative statement" under section 403(r)(3)(C) of the act because the statement was not published by CDC and is instead the statement of individual employees of CDC made in their individual capacities, as discussed in section I.A.2 of this document.

B. Statement 2

Statement 2 reads: "[Antioxidants] may help prevent disease. Antioxidants fight harmful molecules called oxygen free radicals, which are created by the body as cells go about their normal business of producing energy * * * [Some] studies show that antioxidants may help prevent heart disease, some cancers, cataracts, that are more common as people get older." The notification identified Statement 2 as an "authoritative statement" for purposes of making the claim that is the subject

of this rulemaking. The statement is found within an information piece entitled "Life Extension: Science or Fiction?" that is provided on the Internet by the Administration on Aging and which includes statements from the "Age Page" of the National Institute on Aging (an Institute of NIH) ("<http://www.aoa.dhhs.gov/aoa/pages/agepages/lifextsn.html>" accessed on 12/2/97). This electronically available information (submitted to the agency as a hardcopy reprint from the Internet information) is dated 1994, is approximately two standard printed pages in length, and is described as being intended to inform the reader about chemicals being studied that may play a role in aging and what scientists have learned about them so far. Topics covered include antioxidants, deoxyribonucleic acid (DNA), dehydroepiandrosterone (DHEA), and other hormones. Ten tips for healthy aging are also included. The section on antioxidants is 14 sentences in length and includes the three sentences identified as the subject statement. The agency notes that the last sentence of the antioxidant section is: "More research is needed before specific recommendations can be made."

FDA asked NIH whether the statement is an "authoritative statement" under FDAMA. NIH responded to FDA that the statement is not an authoritative statement of NIH because it was prepared by an individual from the National Institute on Aging and is not based on a deliberative review of the scientific evidence regarding the nutrient-disease relationship in question (Ref. 6). Therefore, FDA has concluded that the statement is not an "authoritative statement" under section 403(r)(3)(C) of the act because it is not based on a deliberative review of the scientific evidence, as described in section I.A.3 of this document.

C. Statement 3

Statement 3 reads: "The antioxidant nutrients found in plant foods (e.g., vitamin C, carotenoids, vitamin E, and certain minerals) are presently of great interest to scientists and the public because of their potentially beneficial role in reducing the risk of cancer and certain other chronic diseases." The notification identified Statement 3 as an "authoritative statement" for purposes of making the claim that is the subject of this rulemaking. The statement is from an electronic version of the dietary guidelines issued jointly by DHHS and USDA and provided on the Internet ("<http://www.usda.gov/fcs/library/0102-1.txt>" accessed on 12/5/97). The submitted material consists of selected

pages reprinted from the Internet information, which identifies the seven dietary guidelines and gives background information on the use of, and reasons for, the guidelines. The dietary guidelines reflect the findings of a panel of scientists concerning the dietary recommendations to be made to the U.S. population, and the guidelines are based on a deliberative review of the scientific evidence about the nutrient/disease relationships that the guidelines address. The subject statement is found within the discussion that accompanies the recommendation to "Choose a diet with plenty of grain products, vegetables, and fruits."

The statement indicates that a relationship between antioxidant nutrients and cancer and other chronic disease is "of great interest" because of a "potentially beneficial role." The statement points to the need for future research and suggests that whether a relationship exists should be the subject of scientific study, but does not indicate that there exists a scientifically sound relationship that should be accorded a presumption of validity. This assessment is further supported by the fact that the subject of the dietary guidelines recommendation that the text is intended to clarify is the dietary importance of grain products, vegetables, and fruits, not the specific impact of antioxidant nutrients, vitamins C and E, per se. FDA notes that, consistent with the dietary guidelines, the agency has authorized a health claim for the relationship between cancer and fruits and vegetables that contain vitamin C (as well as vitamin A (as beta-carotene) and dietary fiber) (21 CFR 101.78).

On this basis, FDA has concluded that the statement is not an "authoritative statement" under section 403(r)(3)(C) of the act because the statement indicates that the scientific evidence about the relationship in question is preliminary or inconclusive, as discussed in section I.A.3 of this document.

The dietary guidelines is the product of a periodic review by a group of Federal agencies, the most recent review having been completed in 1995. FDA did not attempt to reconvene this group of Federal agencies to consult with it about whether the statement is an authoritative statement because, as discussed previously, the wording and context of the statement show that it is not an authoritative statement under section 403(r)(3)(C) of the act.

D. Statement 4

Statement 4 reads: "A diet high in fiber, high in antioxidants, and low in fat may play an important role in

preventing the development of atherosclerosis, coronary heart disease, and some cancers." The notification identified Statement 4 as an "authoritative statement" for purposes of making the claim that is the subject of this rulemaking. The statement is found in information on "Health in Later Years" provided on the Internet by CDC's Office of Women's Health in a section entitled: "Health Problems among Older Women," and is included in the subsection "Improving Health and Quality of Life" ("<http://www.cdc.gov/od/owh/whily.htm>" accessed on 11/26/97). This electronically available information (submitted to the agency as a hardcopy reprint from the Internet information) is not dated, is approximately three standard printed pages in length, and covers the topics of coronary heart disease, cancer, stroke, and other diseases.

FDA asked CDC whether this statement is an "authoritative statement" under FDAMA. CDC responded that the statement is not an authoritative statement of CDC because, although it is a statement from CDC, it is not based upon a deliberative review of the scientific evidence regarding the nutrient-disease relationship in question; rather, it is a statement from an educational fact sheet developed by CDC's Office of Women's Health to convey information to the public (Ref. 5). Therefore, FDA has concluded that the statement is not an "authoritative statement" under section 403(r)(3)(C) of the act because the statement is not based on a deliberative review of the scientific evidence.

E. Statement 5

Statement 5 reads: "[It] is likely that certain antioxidants, such as vitamins C and E, may destroy the oxygen radicals, retard molecular damage, and perhaps slow the rate of aging." The notification identified Statement 5 as an "authoritative statement" for purposes of making the claim that is the subject of this rulemaking. The statement is contained in an undated press release from the National Institute on Aging at NIH, which was provided on the Internet ("<http://www.nih.gov/nia/new/press/agingcau.htm>" accessed on 12/1/97). The press release (submitted to the agency as a hardcopy reprint from the Internet) states that it is a synopsis of a recent publication entitled: "Aging—Causes and Defenses," which had been authored by R. Martin, D. Danger, and N. Holbrook and published in *The Annual Review of Medicine* (44:419,429:1993). The press release indicates that it is providing a synopsis

of the publication but does not clarify if the authors are associated with, or are staff of, NIH. *The Annual Review of Medicine* is published periodically by Annual Reviews, Inc., in Palo Alto, CA. Editors for each volume serve as reviewers for the various articles included in the volume and contributors are asked to submit articles to be considered for publication.

The statement is not "about the relationship between a nutrient and a disease or health-related condition" because aging, the absence of oxygen radicals, and the presence of molecular damage are not diseases or health-related conditions. FDA has therefore concluded that the statement does not address a disease or health-related condition and therefore, as discussed in section I.A.1 of this document, is not an "authoritative statement" under section 403(r)(3)(C) of the act.

F. Statement 6

Statement 6 reads: "Antioxidants are thought to help prevent heart attack, stroke and cancer." The notification identified Statement 6 as an "authoritative statement" for purposes of making the claim that is the subject of this rulemaking. The statement is found in *Human Nutrition* (quarterly reports of selected research projects, 4th quarter 1996) issued by the USDA's ARS and provided on the Internet ("<http://www.ars.usda.gov/is/qtr/q496/hn496.htm>" accessed on 12/3/97). *Human Nutrition* is a periodic compilation of brief (one paragraph) descriptions of ongoing research being conducted within the various ARS facilities. The subject statement (submitted to the agency as a hardcopy reprint from the Internet) appears in a description of research entitled: "Do carotenoids—the bright red, yellow and orange pigments in fruits and vegetables—warrant a Recommended Dietary Allowance?" The paragraph describes the nature and outcome of two ARS studies and is attributed to Betty J. Burr at the USDA Western Human Nutrition Research Center in San Francisco. The agency notes that the last sentence of the paragraph is: "Further ARS studies will try to shed more light on whether a specific minimum daily intake of carotenoids is important for good health."

The context of the paragraph, as well as the wording of the statement (i.e., "are thought"), suggests that the scientific evidence about the relationship in question is preliminary or inconclusive.

The agency asked USDA whether the statement is an "authoritative statement" under FDAMA. USDA

responded to FDA that the statement is not an authoritative statement of USDA because it was not based upon a deliberative review of the scientific evidence regarding a relationship between the nutrient and the disease in question (Ref. 7). USDA explained that the ARS quarterly reports describe progress on individual projects without a deliberative review of all relevant scientific evidence. Therefore, FDA has concluded that the statement is not an "authoritative statement" under section 403(r)(3)(C) of the act because it is not based on a deliberative review of the scientific evidence.

In summary, FDA has concluded that the notification does not include any authoritative statement published by a scientific body as required by section 403(r)(3)(C) of the act. Accordingly, the subject claim relating to the relationship between antioxidant vitamins C and E and the risk in adults of atherosclerosis, coronary heart disease, certain cancers, and cataracts is not authorized under section 403(r)(3)(C) of the act and is, therefore, prohibited. The agency notes that, at any future time, a notification may be submitted to the agency that bases such a claim or claims on a statement that meets the requirements of section 403(r)(3)(C) of the act. If there is no authoritative statement that may serve as a basis for such claims, an interested person may petition the agency under section 403(r)(4) of the act and § 101.70 to authorize the health claim or claims by regulation under section 403(r)(3)(B) of the act.

IV. Issuance of an Interim Final Rule, Immediate Effective Date, and Opportunity for Public Comment

For the reasons described in this section of this document, FDA is issuing this rule as an interim final rule, effective immediately, with an opportunity for public comment. New section 403(r)(7)(B) of the act (21 U.S.C. 343(r)(7)(B)), added by section 301 of FDAMA, provides that FDA "may make proposed regulations issued under [section 403(r)] effective upon publication pending consideration of public comment and publication of a final regulation" if the agency "determines that such action is necessary * * * to enable [FDA] to act promptly to ban or modify a claim" under section 403(r) of the act. For purposes of judicial review, "[s]uch proposed regulations shall be deemed final agency action." The legislative history indicates that the agency should issue rules under this authority as interim final rules (H. Conf. Rept. 105-399, at 98 (1997)).

As described in section III of this document, FDA has determined that the statements submitted in support of the prospective health claim do not meet the requirements for authoritative statements in section 403(r)(3)(C) of the act. FDA has determined that it is necessary to act promptly to prohibit the claim's use under section 403(r)(3)(C) of the act, and accordingly, is issuing this interim final rule to ban its use under section 403(r)(3)(C).

FDA invites public comment on this interim final rule. The agency will consider modifications to this interim final rule based on comments made during the comment period. Interested persons may, on or before September 8, 1998, submit to the Dockets Management Branch (address above) written comments regarding this interim final rule. Comments must be received by that date. Two copies of any comments are to be submitted, except that individuals may submit one 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 office above between 9 a.m. and 4 p.m., Monday through Friday.

V. Environmental Impact

The agency has determined under 21 CFR 25.30(k) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VI. Analysis of Economic Impacts

A. Benefit-Cost Analysis

FDA has examined the impacts of this interim final rule under Executive Order 12866. Executive Order 12866 directs Federal agencies to assess the costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). According to Executive Order 12866, a regulatory action is "significant" if it meets any one of a number of specified conditions, including having an annual effect on the economy of \$100 million; adversely affecting in a material way a sector of the economy, competition, or jobs; or if it raises novel legal or policy issues. FDA finds that this interim final rule is not a significant regulatory action as defined by Executive Order 12866. In addition, it has been determined that

this interim final rule is not a major rule for the purpose of congressional review.

If in the future FDA authorizes health claims relating to the relationship between antioxidant vitamins C and E and the risk in adults of atherosclerosis, coronary heart disease, certain cancers, and cataracts after finding that there is significant scientific agreement about these relationships, the cost to consumers of prohibiting this claim at this time would be the cost of having kept, in the interim, information from appearing in food labeling that would ultimately be shown to be scientifically valid, truthful, and not misleading. At this time, the benefit to consumers of prohibiting this claim is that a claim that has not been shown to be scientifically valid will not appear in food labeling. Accordingly, consumers will be able generally to have confidence when they read food labeling that any diet-disease relationship information in that labeling has been shown to be scientifically valid.

A health claim relating to the relationship between antioxidant vitamins C and E and the risk in adults of atherosclerosis, coronary heart disease, certain cancers, and cataracts has not been authorized under existing regulations. The prohibition of this claim in this interim final rule results in no regulatory changes for firms, and therefore no costs to firms are attributable to this interim final rule.

B. Small Entity Analysis

FDA has examined the impacts of this interim final rule under the Regulatory Flexibility Act. The Regulatory Flexibility Act (5 U.S.C. 601-612) requires Federal agencies to consider alternatives that would minimize the economic impact of their regulations on small businesses and other small entities. In compliance with the Regulatory Flexibility Act, FDA finds that this interim final rule will not have a significant impact on a substantial number of small entities.

A health claim relating to the relationship between antioxidant vitamins C and E and the risk in adults of atherosclerosis, coronary heart disease, certain cancers, and cataracts has not been authorized under existing regulations. The prohibition of this claim in this interim final rule results in no regulatory changes for firms, and therefore this rule will not result in a significant increase in costs to any small entity. Therefore, this rule will not have a significant economic impact on a substantial number of small entities. Accordingly, under the Regulatory Flexibility Act (5 U.S.C. 601-612), the

agency certifies that this interim final rule will not have a significant economic impact on a substantial number of small entities.

C. Unfunded Mandates Reform Act of 1995

FDA has examined the impacts of this interim final rule under the Unfunded Mandates Reform Act of 1995 (UMRA) (Pub. L. 104-4). This interim final rule does not trigger the requirement for a written statement under section 202(a) of UMRA because it does not impose a mandate that results in an expenditure of \$100 million or more by State, local, and tribal governments in the aggregate, or by the private sector, in any 1 year.

VII. The Paperwork Reduction Act of 1995

This interim final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520) is not required.

VIII. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Commission on Dietary Supplement Labels, "Report of the Commission on Dietary Supplement Labels," November 1997, p. vii.
2. Notification to Donna E. Shalala, DHHS, from Jonathan W. Emord et al., Emord & Associates, P.C., Counsel for Weider Nutrition International, Inc., February 23, 1998.
3. "Food Labeling—Questions and Answers—Volume I—For Guidance to Facilitate the Process of Developing or Revising Labels for Foods Other than Dietary Supplements," August 1993, Questions C1-C54.
4. "Food Labeling—Questions and Answers—Volume II—A Guide for Restaurants and Other Retail Establishments," August 1995, Questions R117-R127.
5. Letter to Christine J. Lewis, CFSAN, FDA, from Dixie E. Snider, CDC, April 21, 1998.
6. Letter to Christine Lewis, CFSAN, FDA, from William R. Harlan, NIH, April 30, 1998.
7. Letter to Christine Lewis, CFSAN, FDA, from Eileen Kennedy, USDA, May 7, 1998.

Dated: June 16, 1998.

William B. Schultz,

Deputy Commissioner for Policy.

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