DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket No. 98N–0428]

Food Labeling: Health Claims; Antioxidant Vitamin A and Beta-Carotene and the Risk in Adults of Atherosclerosis, Coronary Heart Disease, and Certain Cancers

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 vitamin A and beta-carotene and the risk in adults of atherosclerosis, coronary heart disease, and certain cancers. This interim final 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 interim final 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 (21 U.S.C. 343(r)(2) and (r)(3)) 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. 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. FDAMA and its requirements are discussed in more detail in ''Food Labeling: Health Claims; Antioxidant Vitamins C and E and the Risk in Adults of Atherosclerosis, Coronary Heart Disease, Certain Cancers, and Cataracts'' (hereinafter referred to as ''Health Claims; Vitamins C and E''), which is published elsewhere in this issue of the **Federal Register**. In particular, aspects of the requirements for an ''authoritative statement'' that are relevant to this rulemaking and FDA's review process for notifications are discussed in sections I.A and I.B, respectively, of that document.

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. 1). 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 second claim in the notification. The notification included 11 statements that the petitioner identified as authoritative statements on which the following claim is based: ''Antioxidant vitamin A and beta-carotene may reduce the risk in adults of atherosclerosis, coronary heart disease and certain cancers. Sources of Vitamin A and beta-carotene include red, yellow and green leafy vegetables, dairy products, 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 vitamin A and beta-carotene and a number of different diseases and, thus, in point of fact, reflects several prospective health claims. The second sentence, ''Sources of Vitamin A and beta-carotene include red, yellow and green leafy vegetables, dairy products, 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 (21 U.S.C. 321(n)). These aspects of nutrient content claims and dietary guidance are discussed in more detail in ''Health Claims; Vitamins C and E,'' which is published elsewhere in this issue of the **Federal Register**.

III. Basis for the Action

FDA has reviewed the notification submitted in support of the prospective claim: ''Antioxidant vitamin A and beta-carotene may reduce the risk in adults of atherosclerosis, coronary heart disease and certain cancers.'' The agency has determined that none of the 11 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 11 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 report on nutrition monitoring prepared for the Department of Health and Human Services (DHHS) and the U.S. Department of Agriculture (USDA); (2) an electronic version provided on the Internet of ''Nutrition and Your Health: Dietary Guidelines for Americans,''

recommendations developed by a group of Federal agencies and issued jointly by DHHS and USDA; (3) electronic versions provided on the Internet of four quarterly reports from USDA's Agricultural Research Service (ARS) (statement 3, 7, 9, and 11); (4) electronic versions provided on the Internet of two interpretative summaries from USDA/ARS Technology Transfer Information Center (statements 4 and 10); (5) public information provided on the Internet by an institute of the National Institutes of Health (NIH); (6) public information provided on the Internet by USDA/ARS Beltsville Human Nutrition Research Center; and (7) public information provided on the Internet by the National Cancer Institute (NCI), an institute within NIH. Thus, nine statements in the notification are attributable to either NIH or USDA/ARS. A 10th statement is attributable to USDA and DHHS and is intended for use by Federal agencies including NIH, the Centers for Disease Control and Prevention (CDC), and USDA/ARS. An 11th statement from the Dietary Guidelines for Americans is attributable to a group of Federal agencies that included NIH, CDC, and USDA/ARS. Two of the agencies, 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 agencies that were identified as users of the ''Nutrition Monitoring Report'' as well as the group that developed the dietary guidelines included Federal agencies that are such scientific bodies, including NIH, CDC, and USDA/ARS. 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 11 statements discussed in sections III.A through III.K of this document was found to be an authoritative statement.

A. Statement 1

Statement 1 reads: ''Beta-carotene and other pro-vitamin a carotenoids can be converted to vitamin A in the body. Interest in the carotenoids has increased in recent years because of the accumulation of a large body of evidence that foods high in carotenoids are protective against a variety of epithelial cancers.'' 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 a discussion on vitamins that is contained in ''Nutrition Monitoring in the United States—An Update Report on Nutrition Monitoring'' that was prepared for USDA and the Public Health Service of DHHS by the Life Sciences Research Office (SRO) of the Federation of American Societies for Experimental Biology (FASEB) (DHHS Publication No. (PHS) 89–1255, September 1989, 71). The notification provided a photocopy of selected pages from the report.

The statement indicates that there is interest in the relationship because of a growing body of evidence, but does not confirm that the relationship is considered scientifically valid or well established. Rather, the context suggests that further research would be worthwhile and that the scientific evidence about the relationship is preliminary or inconclusive, as described in section I.A.3 of ''Health Claims; Vitamins C and E,'' which is published elsewhere in this issue of the **Federal Register.**

The agency notes that the report was prepared under a DHHS contract by LSRO/FASEB, an organization that is neither a Federal Government agency nor affiliated with the National Academy of Sciences (NAS). Contractual activities involved in the preparation of the report were overseen by several Federal agencies that participate in the National Nutrition Monitoring System (NNMS). The report provides an independent expert panel's review of the dietary and nutritional status of the U.S. population, as well as the factors that determine status, based on information available through the NNMS; the report is an advisory document for the Government agencies. A disclaimer that appears on the inside front cover of the report, which was not included in the notification, states that, although the report was printed and distributed as part of a series of reports from the NNMS, ''the interpretations contained in this report do not necessarily express the views or policies of the U.S. Government and its constituent agencies'' (Ref. 2). Additionally, as noted in the foreword of the report (page vii), representatives of participating Federal Government agencies ''reviewed final drafts of the report for technical accuracy and satisfaction of the scope of work'' (Ref. 2).

Given this disclaimer and the statement from the foreword, the component of the submitter's notification that provided ''a concise description of the basis upon which [the submitter] relied for determining that the requirements of [403(r)(3)(C)(i)] have been satisfied'' (as required by 403(r)(3)(C)(ii)(I) of the act) needed to address why this statement was in fact an authoritative statement. It did not. The disclaimer indicates that Federal Government agencies cannot be considered to have ''published'' the report in the sense that it represents official policy of the agencies, as discussed in section I.A.2 of ''Health Claims; Vitamins C and E,'' which is published elsewhere in this issue of the **Federal Register**. The foreword of the report indicates that it may involve a deliberative review of the scientific evidence about the dietary and nutritional status of the U.S. population, but that it does not involve a deliberative review of the scientific evidence about diet/disease relationships. Further, the foreword indicates that the Federal agencies did not themselves conduct a deliberative review of the scientific evidence necessary for the statements in the report to be ''authoritative statements,'' as described in section I.A.3 of ''Health Claims; Vitamins C and E,'' which is published elsewhere in this issue of the **Federal Register**, but rather only a review for technical accuracy of a final draft of the report itself.

FDA concludes that the statement is not an ''authoritative statement'' because it indicates that the scientific evidence is preliminary or inconclusive, that it does not reflect the official policy of an appropriate scientific body, and that no appropriate scientific body has conducted a deliberative review of the scientific evidence.

B. Statement 2

Statement 2 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 2 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 ''Nutrition and Your Health: Dietary Guidelines for Americans'' (Home and Garden Bulletin No. 232, Fourth Ed., 1995), hereinafter referred to as 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 guideline is the dietary importance of grain products, vegetables, and fruits, not the specific impact of antioxidant nutrients, vitamin A and beta-carotene, 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 vitamins A (as beta-carotene) as well as vitamin C 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 the **Federal Register** ''Health Claims; Vitamins C and E,'' which is published elsewhere in this issue of the **Federal Register**.

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.

C. Statement 3

Statement 3 reads: ''If the findings hold up in further research, eating more vegetables rich in beta-carotene and related carotenoids–lutein and lycopene–may help people ward off a cold or flu as well as protect from cancer * * *. The findings also suggest that carotenoid-rich vegetables also stimulate the immune system.'' 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 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: ''Daily servings of dark green and deep yellow vegetables and tomatoes boost immune response, a preliminary study suggests.'' The paragraph describes the nature and outcome of one ARS study and is attributed to Tim R. Kramer and Beverly Clevidence of the USDA Beltsville Human Nutrition Research Center in Beltsville, MD. The agency notes that the research is identified as a ''preliminary study.''

The context of the paragraph, as well as the wording of the statement (i.e., ''if the findings hold up''), suggests that the statement is based on preliminary research and that further study is needed. As such, the statement appears to indicate that the scientific evidence about the relationship 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. 3). 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)(C)(3) of the act because it is not based on a deliberative review of the scientific evidence.

D. Statement 4

Statement 4 reads: ''This research involving cells provides data which supports the general hypothesis that beta-carotene and lutein protect cells by serving as antioxidants.'' 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 a one paragraph interpretative summary of a research report from Technology Transfer Information Center, TEKTRAN of USDA/ARS entitled ''Beta-carotene and Lutein Protect the Plasma Membrane of HEPG2 Human Liver Cells Against Oxidant-induced Damage,'' and provided on the Internet (''http://www.nalusda.gov/ttic/tektran/data/000006/92/0000069264.html'' accessed on 12/3/97) (ARS Report Number 69264). It describes the nature and outcome of one study, which is attributed to Keith J. Martin, Mark L. Failla, and James C. Smith, Jr.

The statement is not ''about the relationship between a nutrient and a disease or health-related condition'' because no disease is identified in the statement. Therefore, FDA has concluded that the statement does not address a disease or health-related condition and therefore is not an ''authoritative statement'' under section 403(r)(C)(3) of the act, as described in section I.A.1 of ''Health Claims; Vitamins C and E,'' which is published elsewhere in this issue of the **Federal Register**.

E. Statement 5

Statement 5 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 * * *. [S]ome studies show that antioxidants may help prevent heart disease, some cancers, cataracts, and other health problems that are more common as people get older.'' 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 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 the 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, DNA, DHEA, and other hormones. Ten tips for healthy aging are also included. The section on antioxidants is 14 sentences in length and includes the 3 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 scientific evidence regarding the nutrient-disease relationship in question (Ref. 4). 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.

F. Statement 6

Statement 6 reads: ''As potent antioxidants, [lutein and lycopene] are thought to contribute to the lower rates of heart disease, cancer and other diseases of aging among populations that eat a lot of fruits and vegetables.'' 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 within an information piece, ''BHNRC Success Stories,'' provided on the Internet by USDA/ARS Beltsville Human Nutrition Research Center and entitled: ''Carotenoids Show Their Real Colors'' (''http://www.barc.usda.gov/bhnrc/success.htm'' accessed on 12/4/97). This electronically available information (submitted to the agency as a hardcopy reprint from the Internet information) is undated. The section on carotenoids is three brief paragraphs in length and describes the nature and outcome of a single ARS study attributed to Tim Kramer and Beverly Clevidence. The same study was also referenced in ARS's *Human Nutrition* quarterly report as noted in the discussion of statement 3 in section III.C of this document.

The context of the section, as well as the wording of the statement (i.e., ''are thought''), suggests that the statement is based on preliminary research and that further study is needed. As such, the statement appears to indicate that the scientific evidence about the relationship 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. 3). USDA explained that the ARS ''BHNRC Success Stories'' 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)(C)(3) of the act because it is not based on a deliberative review of the scientific evidence.

G. Statement 7

Statement 7 reads: ''Researchers also found more evidence suggesting that carotenes act as antioxidants to protect the body from harmful oxidation. Antioxidants are thought to help prevent heart attack, stroke and cancer. During the low-carotene stints, researchers recorded several biochemical signs of oxidative damage.'' The notification identified statement 7 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) (see discussion of statement 3 in section III.C of this document), which is 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) 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 Burri of the Western Human Nutrition Research Center in San Francisco, CA. The agency notes that the final sentence states: ''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 statement is based on preliminary research and that further study is needed. As such, the statement appears to indicate that the scientific evidence about the relationship 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. 3). Therefore, FDA has concluded that the statement is not an ''authoritative statement'' under section 403(r)(C)(3) of the act because it is not based on a deliberative review of the scientific evidence.

H. Statement 8

Statement 8 reads: ''[H]igh dietary carotene and possibly vitamins C and E and folate are associated with reduced risk for cervical cancer.'' The notification identified statement 8 as an ''authoritative statement'' for purposes of making the claim that is the subject of this rulemaking. The statement is found in information provided on the Internet by the NCI, an institute of NIH, in an article entitled: ''Prevention of Cervical Cancer'' and disseminated as part of ''PDQ—Detection & Prevention—Health Professionals'' (PDQ stands for physicians data query) (''http://cancernet.nci.nih.gov/ clinpdq/screening/ Prevention__of__cervical__cancer__Physician.html'' accessed on 12/1/97). This electronically available information (submitted as a hardcopy reprint from the Internet information) is undated, approximately nine standard printed pages in length, and is described as intended for use by doctors and other health care professionals. The subject sentence is one of several sentences summarizing research on the intake of micronutrients and the risk of squamous intraepithelial lesion (SIL) and cervical cancer.

FDA asked NIH whether this was an ''authoritative statement'' under FDAMA. NIH responded that the statement was not an authoritative statement of NIH and does not reflect consensus within NIH (Ref. 4). NIH explained that the evidence was reviewed by an editorial board for PDQ, and the majority of the members are not Federal employees. The statements contained in PDQ were reported by NIH to be ''state of the art'' educational statements developed by an editorial board that assesses the levels of scientific evidence supporting the statements. In this instance, the scientific evidence for the nutrient-disease relationship was not considered to be strong since it was based on observational studies. NIH reiterated that the statement is not the product of consensus process within the NCI and the statement has not undergone formal review and clearance by the Director of the National Institutes of Health.

Therefore, FDA has concluded that the statement is not an ''authoritative statement'' under section 403(r)(C)(3) of

the act because it does not reflect consensus within NIH, as discussed in section I.A.2 of ''Health Claims: Vitamin C and E,'' which is published elsewhere in this issue of the **Federal Register**.

I. Statement 9

Statement 9 reads: ''[B]eta carotene or vitamin A supplements have reversed pre-cancerous conditions in people's mouths.'' The notification identified statement 9 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, 3rd quarter 1995) (see discussion of statement 3 in section III.C of this document), which is issued by the USDA's ARS and provided on the Internet (''http://www.ars.usda.gov/is/qtr/q395/hn395.htm'' accessed on 12/3/97) in a description of research entitled: ''A daily dose of blue-green algae Spirulina may help prevent cancer of the mouth, a study shows.'' The paragraph describes the nature and outcome of an ARS study and is attributed to Padmanabhan P. Nair of the Beltsville Human Nutrition Research Center, Beltsville, MD.

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. 3). Therefore, FDA has concluded that the statement is not an ''authoritative statement'' under section 403(r)(C)(3) of the act because it is not based on a deliberative review of the scientific evidence.

J. Statement 10

Statement 10 reads: ''Carotenoids or other plant components appear to boost the immune system.'' The notification identified statement 10 as an ''authoritative statement'' for purposes of making the claim that is the subject of this rulemaking. The statement is found in a one-paragraph interpretative summary of a research report from Technology Transfer Information Center, TEKTRAN of USDA/ARS entitled: ''Consumption of Carotenoid-Rich Vegetables Increases T-Lymphocyte Proliferation and Plasma Levels of Carotenoid Oxidation Products'' and provided on the Internet (''http://www.nalusda.gov/ttic/tektran/data/000007/41/0000074185.html'' accessed on 12/3/97) (ARS Report Number 74185). It describes the nature and outcome of one study, which is attributed to ten researchers, the first author being Beverly Clevidence.

FDA finds that the statement is not ''about the relationship between a nutrient and a disease or health-related condition'' because no disease is identified in the statement. Therefore, FDA has concluded that the statement does not address a disease or health-related condition and therefore is not an ''authoritative statement'' under section 403(r)(C)(3) of the act.

K. Statement 11

Statement 11 reads: ''A wealth of epidemiological evidence has linked a high intake of green leafy and deep yellow vegetables—both rich in beta-carotene—with lower rates of many types of cancer * * *. Men over 65 who took a 50-milligram beta-carotene supplement every other day during the 12-year study had natural killer cells that were more active than their counterparts who got a placebo. Natural killer cells—or NK cells—are the immune system's sentinels, ever on watch for viruses and cancer cells.'' The notification identified statement 11 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) (see discussion of statement 3 in section III.C of this document), which is 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) in a description of research entitled: ''Older people who get plenty of beta carotene may have a better chance of preventing virus infections or a cancerous growth.'' The paragraph describes the nature and outcome of a study and is attributed to Simin Nikbin Meydani of the USDA Human Nutrition Research Center on Aging at Tufts, Boston, MA.

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. 3). Therefore, FDA has concluded that the statement is not an ''authoritative statement'' under section 403(r)(C)(3) 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 statements 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 vitamin A and beta-carotene and the risk in adults of atherosclerosis, coronary heart disease, and certain cancers 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) and 21 CFR 10.70 to authorize the health claim or claims by regulation under section 403(r)(3)(B).

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, 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. No. 105–399, at 98 (1997)).

As described previously 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 vitamin A and beta-carotene and the risk in adults of atherosclerosis, coronary heart disease, and certain cancers 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 vitamin A and beta-carotene and the risk in adults of atherosclerosis, coronary heart disease, and certain cancers 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 related to the relationship between antioxidant vitamin A and beta-carotene and the risk in adults of atherosclerosis, coronary heart disease, and certain cancers 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 interim final rule will not result in a significant increase in costs to any small entity. Therefore, this interim final 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. 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.

2. LSRO, FASEB, ''Nutrition Monitoring in the United States—An Update Report on Nutrition Monitoring,'' prepared for USDA and DHHS, DHHS Pub. No. (PHS) 89–1255, PHS, DHHS, U.S. Government Printing Office, Washington, DC, inside front cover and pp. iii to vii, September, 1989.

3. Letter to Christine Lewis, CFSAN, FDA, from Eileen Kennedy, USDA, May 7, 1998.

4. Letter to Christine Lewis, CFSAN, FDA, from William R. Harlan, NIH, April 30, 1998.

Dated: June 16, 1998.

William B. Schultz,

Deputy Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket No. 98N–0427]

Food Labeling: Health Claims; B-Complex Vitamins, Lowered Homocysteine Levels, and the Risk in Adults of Cardiovascular Disease

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 B-complex vitamins (folic acid, vitamin B_6, vitamin B_{12}), lowering elevated serum homocysteine levels, and the risk in adults of cardiovascular disease. This interim final 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