

CSPI

Center for
Science in the
Public
Interest

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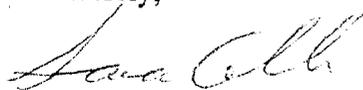
Dockets Management Branch
Food and Drug Administration
Room 1061
5630 Fishers Lane,
Rockville, MD 20852

To Whom it May Concern:

Please file the enclosed Citizen Petition for Amendment of the Final Regulation on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, submitted by the Center for Science in the Public Interest.

Please call 202-332-9110, extension 362 with any questions. Thank you.

Sincerely,



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IH-D-6

March 30, 2000

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Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Citizen Petition

The undersigned submits this petition under §§ 403(a), 403(r)(6), and 701(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) to request that the Commissioner of Food and Drugs amend the Final Regulation on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body (Docket No. 98N-0044).

I. Action Requested

The Center for Science in the Public Interest (CSPI)¹ requests that the Food and Drug Administration (FDA) modify language in the Preamble to the above-referenced rule to prohibit dietary supplements from carrying the same claims as those that are approved for over-the-counter (OTC) drugs.

At a minimum, the FDA should require that all structure/function claims for dietary supplements that also appear on OTC drugs be prefaced by the words “may,” “might” or “may be.” In the alternative, dietary supplements should be required to carry a statement such as:

¹ CSPI is a nonprofit organization based in Washington D.C. that is supported by almost one million members who subscribe to its *Nutrition Action Healthletter*. CSPI has been working to improve the public's health through better nutrition and safer food since 1971.

“This product is not an over-the-counter drug. The U.S. Food and Drug Administration has not determined whether the product is safe.”

II. Statement of Grounds

On April 29, 1998, the FDA issued a proposed Regulation on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body.² The proposal did not address the permissibility of using label claims on dietary supplements that had been previously approved for OTC drugs, and the FDA received only three comments which raised this issue. Notwithstanding the lack of adequate notice and the paucity of public comments on this issue, the preamble to the FDA’s final rule specified a list of approved claims for OTC drugs that may also be used for dietary supplements.³ Under the final rule, for example, dietary supplements may claim on the label that the product can be used for “the occasional relief of sleeplessness,” “occasional simple nervous tension,” and “for the prevention and treatment of the nausea, vomiting or dizziness associated with motion” -- all of which are claims also permitted on OTC drug labels.⁴

While CSPI does not necessarily favor the use of OTC drugs over dietary supplements, it believes that permitting the labels of both products to carry the same claims is false and misleading. Dietary supplements and OTC drugs are often sold side-by-side in indistinguishable containers. The presence of identical claims may lead consumers to presume that such products

² 63 Fed. Reg. 23624 (Apr. 29, 1998).

³ 65 Fed. Reg. 1000 (Jan. 6, 2000). See Appendix A.

⁴ 65 Fed. Reg. at 1031.

are interchangeable, when in fact, OTC drugs have met rigorous safety and effectiveness standards and dietary supplements have not. While many structure/function claims for dietary supplements imply a higher level of substantiation than what actually exists, the use on a dietary supplement of a claim that is identical to an approved claim for an OTC drug exacerbates the degree and likelihood of deception.

Although dietary supplements are required by statute to carry a disclaimer that the *claim* has not been evaluated by the FDA, the use of a claim that is identical to a definitive OTC drug label statement and that appears on a similarly packaged product undermines the impact of the disclaimer. Moreover, there is no comparable disclaimer requirement with respect to ingredient *safety*. Thus, consumers may be led to believe that the supplement is just as safe as its OTC counterpart, even though OTC drugs have met strict standards that do not apply to dietary supplements.

Consumers are not aware of the vast regulatory differences between OTC drugs and dietary supplements. It is incumbent upon the FDA to ensure that labels for each product are readily distinguishable and that the significance of the regulatory distinction between product categories is communicated to the public. The FDA's decision to permit identical claims for OTC drugs and dietary supplements, however, makes it exceedingly difficult for consumers to distinguish supplements from OTC drugs and to understand the ramifications of that distinction.

The agency's policy is thus inconsistent with section 403(a) of the Food, Drug, and Cosmetic Act, 21 U.S.C. §343(a), and is arbitrary and capricious in violation of the Administrative Procedure Act, 5 U.S.C. § 706(2)(A).

A. Dietary supplements and OTC drugs should not carry identical claims because they are subject to different levels of regulatory control.

1. OTC drugs are subject to much greater regulatory scrutiny for safety and effectiveness than dietary supplements.

The FDA's decision to permit identical claims to be made for highly regulated OTC drugs and largely unregulated dietary supplements may mislead consumers into thinking that dietary supplements are as safe and effective as OTC drugs. As Commissioner Jane E. Henney recently testified at a Senate hearing: "When consumers buy food items, drugs, or medical devices, they're purchasing not only the product itself, but FDA's implicit assurance that the product is safe."⁵

OTC drugs may be marketed in one of two ways. First, many are marketed in accordance with the monograph⁶ applicable to that particular type of product, e.g., antacids, nighttime sleep aids, stimulants, etc. The monograph specifies ingredients that are generally recognized as safe and effective at designated dosages, indicates required warnings, and standardizes the claims that may be used. A consumer purchasing this product can be assured that the drug has met appropriate safety and effectiveness standards for a particular use and that the label contains appropriate warning statements.

Furthermore, some OTC drugs may be marketed pursuant to a new drug application

⁵ Jane E. Henney, Ph.D., Commissioner of Food and Drugs, testimony before the U.S. Senate Committee on Appropriations, Subcommittee on Agriculture, Rural Development and Related Agencies, March 7, 2000 <<http://www.fda.gov/ola/2000budget2001.html>>.

⁶ Although the majority of the monographs have been finalized, some have still not reached that stage. The FDA has banned most ingredients that have been characterized as not safe or effective, or where the evidence is insufficient to determine safety or efficacy. 21 C.F.R. § 310.545. Products not yet subject to a final monograph may remain on the market and are not subject to enforcement action unless they pose safety hazards.

(NDA). This process requires thorough pre-market and post-market controls to assure the safety and efficacy of the product and the appropriateness of the labeling.

By contrast, dietary supplements are not subject to such requirements and may be marketed without general recognition of safety and effectiveness.⁷ Unlike the OTC monograph system where claims are evaluated in the context of the safety and effectiveness of ingredients intended for specified uses, dietary supplement claims are evaluated in the abstract. All the FDA determines when (and if)⁸ it receives a 30-day post-market notification is that a particular claim is not a prohibited claim, not whether the claim is true or the product is safe and effective.⁹

This system is inadequate to ensure public safety. On numerous occasions, the FDA has issued alerts concerning the dangers presented by particular dietary supplements,¹⁰ and the

⁷ Manufacturers must provide the FDA with notification of “new” dietary supplement ingredients 75 days prior to marketing but need not gain agency approval. FDCA § 413 (a)(2), 21 U.S.C. 350b (a)(2). Dietary supplement ingredients on the market prior to October 15, 1994 generally receive no systematic agency review at all. FDCA § 413(c), 21 U.S.C. § 350b (2)(c).

⁸ According to recent news reports, the FDA receives 30-day post-market notifications of structure/function claims in only about ten percent of the cases in which the law requires the manufacturer to submit such notifications, *see*, Chris Adams, *Splitting Hairs on Supplement Claims*, Wall St. J., Feb. 22, 2000, at B1.

⁹ The FDA has drawn hairsplitting distinctions between permissible and impermissible claims which are lost on consumers. For example, a claim that a product “supports the immune system” is a permissible structure/function claim. But a claim to “support the body’s antiviral capabilities” is viewed as an impermissible disease claim. Similarly, a claim to “help to maintain cholesterol levels that are already within normal range” is permissible. But it is impermissible to claim that a product “lowers cholesterol,” or “maintains healthy cholesterol.” Final Rule, 65 Fed. Reg. at 1029, 1019.

¹⁰ Most recently, the FDA issued a Public Health Advisory on the risk of drug interactions with St. John’s wort, a popular herb for the treatment of depression. The notice followed the report of a National Institutes of Health study published in *The Lancet*. Researchers discovered a significant interaction between the supplement and protease inhibitors used to treat HIV infection. Based on this study and reports in the medical literature, the FDA advised health

medical community has voiced its concerns.¹¹ In light of the growing evidence that some supplement ingredients may be hazardous, permitting the same claims to appear on both unregulated dietary supplement and highly regulated OTC drug labels may mislead consumers as to the distinctions between regulatory categories and the significance of those distinctions. Consumers should not be led to believe that dietary supplements are as safe and effective as OTC drugs when they are not. But by permitting OTC and dietary supplements to carry the same claims, the FDA fosters that misperception. Thus, the portion of the preamble to the agency's final rule that addresses the use of OTC drug claims on dietary supplements is inconsistent with the prohibition on false and misleading labeling found in section 403(a) of the FDCA and should be rescinded.

2. OTC drugs are subject to GMP regulations.

Good Manufacturing Practice (GMP) regulations require OTC drug manufacturers to maintain consumer-complaint files and written procedures for addressing such complaints.¹²

care practitioners to alert patients to the fact that St. John's wort may also interact with other drugs that are similarly metabolized. The Agency warned that potential drug interactions may occur with respect to drugs used for heart disease, depression, seizures, transplant rejection, as well as oral contraceptives. FDA, Public Health Advisory, Subject: Risk of Drug Interactions with St. Johns's Wort and Indinavir and Other Drugs, Feb. 10, 2000.

¹¹ The American Medical Association (AMA) passed a resolution to work with Congress to give FDA the authority to test new and existing dietary supplements for safety and efficacy. The resolution also pledged that the AMA would seek a label warning consumers of the possibility of "significant side effects and/or interactions with medications and other dietary supplements." *More Oversight Urged for Diet Supplements; Delegates Call for Stepped Up Regulation in Response to Growing Concerns about Dietary Supplements and Herbal Remedies*, American Medical News, <http://www.ama-assn.org/sci-pubs/amnews/pick_00/gvsvd0103.htm> (Jan. 3, 2000).

¹² 21 C.F.R. § 211.198.

During routine inspections, the FDA checks complaint files at drug companies to ensure that such files are maintained and that notices of adverse events are reported to the FDA when appropriate.¹³ With respect to drugs, the FDA has broad authority to inspect “all things therein,” including “records, files, papers, processes, controls and facilities.”¹⁴

In contrast, GMP regulations for dietary supplements have not even been proposed. If and when such regulations are issued, they must, by law, be based on GMPs for foods which do not require manufacturers to maintain complaint files or have a process for addressing complaints.¹⁵ The Special Nutritionals Adverse Event Monitoring System remains voluntary, and for dietary supplements the agency may only inspect equipment, finished and unfinished materials, and labeling.¹⁶

The FDA is thus much less likely to learn of adverse reactions to dietary supplements than of those to OTC drugs and simply cannot ensure the public that the two types of products are subject to a comparable level of safety. As a recent lawsuit demonstrates, the FDA was not informed of 3,500 customer complaints that had been filed with a firm in Utah that marketed an

¹³ Currently, only manufacturers of OTC drugs approved pursuant to an NDA are subject to the mandatory filing of Adverse Event Reports. The FDA, however, plans to propose a rule to extend this requirement to all OTC drugs.

¹⁴ FDCA § 704(a)(1)(A), 21 U.S.C. § 374 (a)(1)(A). The Food and Drug Administration Modernization Act (FDAMA) amended the FDCA to expand the scope of the Agency’s inspection authority over OTC drugs so that it is equal to the broad authority which it has been given for prescription drugs. FDAMA § 407(b), codified at FDCA § 704(a)(1)(B), 21 U.S.C. § 374 (a)(1)(B).

¹⁵ FDCA § 402(g)(2), 21 U.S.C. § 342(g)(2); 21 C.F.R. § 21 C.F.R. § 110.

¹⁶ FDCA § 704(a)(1)(B), 21 U.S.C. § 374 (a)(1)(B).

ephedra-based diet regimen.¹⁷ Thus, without authority comparable to that which it has over OTC drugs, the FDA cannot assure the public that it has received, and that an appropriate regulatory action was taken in response to, consumer complaints. Allowing the same claims for such products under such circumstances is highly misleading: in light of the presence of identical claims on the label, consumers may believe that dietary supplements meet the same safety standards as OTC drugs.

In addition, GMP regulations for drugs ensure the identity, quality, strength, and purity of the products. A recent survey by *Consumer Reports* indicates the same cannot be said for dietary supplements. The survey found that the percentages of particular ingredients often varied significantly from bottle to bottle.¹⁸ Such surveys indicate that the quality of dietary supplements cannot be assured. Thus, until dietary supplements are manufactured in accordance with the same quality standards as those for OTC drugs, it is improper for the FDA to permit the same claims to appear on the labels of dietary supplements and OTC drugs.

B. FDA has acknowledged that a higher level of scrutiny applies to OTC drugs but, nevertheless, allows dietary supplements to make OTC claims.

In the preamble to the final rule, the FDA noted the key differences between OTC and dietary supplements, including the fact that only OTC drugs have been thoroughly reviewed for safety and efficacy. As the preamble explains, that while in a number of instances dietary supplements may make the same claims as certain OTC drugs, OTC drugs may not make claims permitted for dietary supplements unless the Agency determines the claims are appropriate.

¹⁷ Kenneth Howe, *FDA Stops Tracking Herbal Remedies; Agency says it doesn't have the funding to assess adverse reactions*, San Francisco Chronicle, Feb. 14, 2000.

¹⁸ *Herbal Rx The Promise and Pitfalls*, Consumer Reports, March 1999, at 44, 47.

Thus, for example, the FDA stated that it would not permit OTC laxatives to make claims made by dietary supplements that purport to help maintain regularity because higher safety and efficacy standards apply to OTC drugs. The agency explained:

The fact that 'helps maintain regularity' is an acceptable structure/function claim does not mean that it satisfies the requirements for inclusion in an OTC monograph, *including the requirement of a finding of general recognition of safety and effectiveness.*¹⁹

Thus, by its own admission, the FDA recognizes that OTC drugs are held to a higher standard than dietary supplements, yet the agency has approved a regulatory plan that will allow the same label claims for both products. Consumers with a malady that lends itself to treatment by OTC drugs may decide that they are better off taking the "natural" product -- a dietary supplement -- particularly in light of the fact that the supplement makes the same claims as the OTC product.

By permitting various OTC claims to be used on supplements, the FDA has suggested a parity between products that is usually belied by the facts. Such action is arbitrary and capricious in violation of the Administrative Procedure Act, 5 U.S.C. § 706 (2)(A). *See Motor Vehicle Mfrs. Ass'n v. State Farm Auto. Ins. Co.*, 463 U.S. 29 (1983).

III. Environmental Impact

This petition is subject to a categorical exclusion under 21 C.F.R. § 25.30(h) and therefore, CSPI is not required to prepare an environmental assessment or an environmental impact statement.

¹⁹ 65 Fed. Reg. at 1033 (emphasis added).

IV. Economic Impact

No statement of economic impact is required at this time.

V. Conclusion

For the foregoing reasons, CSPI requests that the agency modify the preamble to its final rule to ensure that OTC claims may not appear on dietary supplement labels until such time as dietary supplements are held to standards comparable to those for OTC drugs. At a *minimum* the FDA should require that all structure/function claims for dietary supplements that also appear on OTC drugs should be prefaced by the words “may,” “might” or “may be.” For example, a claim for an OTC antacid states: “For the relief of sour stomach.”²⁰ However, an antacid claim for a dietary supplement should be limited to stating “*May* help relieve sour stomach” until such time as the company has demonstrated that the supplement ingredients are in fact effective.

In the alternative, dietary supplements should be required to carry a statement such as: “This product is not an over-the-counter drug. The U.S. Food and Drug Administration has not determined whether this product is safe.” This statement should immediately follow the disclosure required by section 403(r)(6)(C) of the FDCA that the agency has not evaluated the effectiveness of the product for its claimed uses.²¹

VI. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this

²⁰ 21 C.F.R. § 331.30 (b).

²¹ 21 U.S.C. § 343(r)(6)(C). This section requires dietary supplement labels to advise consumers that a structure/function claim “has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.”

petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to this petition.

Respectfully submitted,

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APPENDIX A

Statements That Qualify As Structure/Function Claims That Have Previously Been Approved for OTC Drugs*

I. Antacids Monograph Claims

- Relief of sour stomach
- Relief of upset stomach

II. Antiflatulents Monograph Claims

- Alleviates the symptoms referred to as gas
- Alleviates bloating
- Alleviates pressure
- Alleviates fullness
- Alleviates stuffed feeling

III. Antiemetics Monograph Claims

- For the prevention and treatment of nausea, vomiting, or dizziness associated with motion

IV. Nighttime Sleep-Aids Monograph Claims

- For the relief of occasional sleeplessness

V. Stimulants Monograph Claims

- Helps restore mental alertness or wakefulness when experiencing fatigue or drowsiness

VI. Daytime Sedatives

- Occasional simple nervous tension
- Nervousness due to common everyday overwork and fatigue
- A relaxed feeling
- Calming down and relaxing
- Gently soothe away the tension
- Calmative
- Resolving that irritability that ruins your day
- Helps you relax
- Restlessness
- Nervous irritability
- When you are under occasional stress, helps you work relaxed

*Food and Drug Administration Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body; Final Rule, 65 Fed. Reg. 999, 1031 (Jan. 6, 2000).

VII. Products for Certain Uses Monograph Claims

- Digestive aid
- Stool softener
- Weight control
- Menstrual
- Laxative

VIII. Products for the Treatment and/or Prevention of Nocturnal Leg Muscle Cramps Monograph Claims

- Treatment and/or prevention of nocturnal leg muscle cramps, i.e. a condition of localized pain in the lower extremities usually occurring in middle life and beyond with no regular pattern concerning time or severity.