

American Medical Association

Physicians dedicated to the health of America



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August 19, 1999

Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

RE: Dietary Supplements; Center for Food Safety and Applied Nutrition Strategy
[Docket No. 99N-1174]

The American Medical Association (AMA), representing approximately 300,000 physicians and physicians-in-training, is pleased to comment on the Food and Drug Administration's (FDA) request for comments that will assist the Center for Food Safety and Applied Nutrition (CFSAN) to develop an overall strategy for achieving effective regulation of dietary supplements, 64 Fed. Reg. 117, pp. 32880-32881 (June 18, 1999).

The physician members of the AMA are concerned about the quality, safety, and efficacy of dietary supplement products, especially herbal remedies. Many of the AMA's concerns have been communicated to the FDA in three prior letters, dated August 26, 1998, May 27, 1999, and August 4, 1999. Copies of the AMA's letters are enclosed.

The AMA believes that the primary problem is the Dietary Supplement Health and Education Act of 1994 (DSHEA), which failed to provide for adequate regulatory oversight of these dietary supplement products by the FDA. In that regard, our House of Delegates (AMA's policy-making body) has asked the AMA to work with Congress to modify the DSHEA to require that dietary supplements and herbal remedies, including those products already in the marketplace, undergo FDA approval for evidence of safety and efficacy; meet standards established by the United States Pharmacopeia (USP) for identity, strength, quality, purity, packaging, and labeling; and meet FDA postmarketing requirements to report adverse events, including drug interactions.

In the absence of modifications to current federal law, the AMA believes the FDA has the responsibility to do its utmost to protect the health of the public by regulating dietary supplements to the greatest extent possible. The AMA believes that the CFSAN strategy to regulate dietary supplements as effectively as possible under current law must focus on three broad areas: 1) CFSAN must ensure that consumers readily understand the differences between drug products and dietary supplement products (particularly herbal remedies) so each type of product is used appropriately; 2) CFSAN must ensure that dietary supplements are of high quality and have a safety profile that warrants direct purchase by consumers without health professional supervision; and 3) to the extent possible, CFSAN must ensure that structure/function claims for dietary supplements can be substantiated by good science. CFSAN should work closely with the Center for Drug Evaluation and Research (CDER) in coordinating FDA's regulatory approach to dietary supplement products.

99N-1174

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1. CFsAN must ensure that consumers readily understand the differences between drug products and dietary supplement products (particularly herbal remedies) so each type of product is used appropriately. In the United States, drug products are used to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases. Drug products have a known benefit/risk ratio based on rigorous scientific study and premarket regulatory review by the FDA. In contrast, knowledge about the benefit/risk ratio of dietary supplements is far less certain, and the scientific evidence to support the claims for these products is not reviewed by the FDA prior to marketing. In large part, it is for this reason that dietary supplement labeling cannot make disease claims, but is limited to structure/function claims. Thus, it is imperative that dietary supplement products are not used inappropriately by consumers to treat diseases or delay individuals with diseases from obtaining a diagnosis and appropriate drug treatment from a physician.

The AMA is deeply troubled by the FDA Notice of July 8, 1999 [Docket No. 98N-0044], published in the Federal Register that suggests the FDA may lower its proposed regulatory standards on structure/function claims that can be made by manufacturers of dietary supplements. Narrowing the definition of disease and/or allowing dietary supplements to make implied disease claims or claims for abnormal conditions associated with natural states will further blur the distinction between a drug and a dietary supplement, increase confusion among consumers regarding appropriate therapies, and diminish the FDA's ability to protect the health of the public. The AMA urges the FDA to hold firm to its Proposed Rule of April 29, 1998, which provided more appropriate definitions and examples of the types of statements that could be made by a manufacturer concerning the effect of a dietary supplement on the structure and function of the body. Please refer to the AMA's letters, dated August 26, 1998, and August 4, 1999, for our detailed comments on this subject.

The DSHEA requires that a structure/function claim for a dietary supplement be followed by the disclaimer: "*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.*" This should help consumers distinguish between drug and dietary supplement products so that each type of product is used appropriately. However, at the FDA's Public Meeting on June 8, 1999, the testimony presented suggests that consumers are disregarding this disclaimer and are using dietary supplements to treat disease. Therefore, when there is evidence that suggests a dietary supplement is being used inappropriately for a specific disease, disorder, or condition, i.e., like a drug, the FDA should require that the label contain an additional warning statement against the use of the dietary supplement product for that use. For example, St. John's Wort frequently has been suggested as a remedy to treat depression. However, the science to support this claim has never been subjected to FDA review. Thus, labeling for dietary supplement products containing St. John's Wort should be required to carry the following:

"WARNING: Dietary supplement products containing St. John's Wort have not been approved by the Food and Drug Administration for the treatment of depression. Individuals who have or think they have depression should not use this product without first consulting a physician."

Similarly, if contraindications to the use of a dietary supplement are known (e.g., use of comfrey in individuals with liver disease), this information also should be included in the labeling.

Finally, the AMA recommends that the FDA develop an extensive educational campaign to inform consumers about the differences between drug products and dietary supplement products. Part of this campaign should include research on dietary supplement use, with the goal of obtaining data on consumer decision-making about using these products.

It is imperative that consumers have the necessary knowledge to know the limitations of dietary supplement products and when they should contact a physician to be appropriately diagnosed and treated with drugs that have known effectiveness for the treatment of diseases, disorders, and conditions. The lack of adequate information on the efficacy, adverse reactions, and interactions of dietary supplements hinders informed decision-making by consumers.

2. CFSAN must ensure that dietary supplements are of high quality and have a safety profile that warrants direct purchase by consumers without health professional supervision. Dietary supplement products will be used primarily by healthy individuals without health professional supervision, and it is imperative that the risks of these products are minimal for this population. Thus, the FDA must ensure that dietary supplement products actually contain the ingredient(s) (and strength[s]) that the manufacturers claim on the labeling, and that these products are manufactured using Good Manufacturing Practices (GMP). Furthermore, the FDA must carefully monitor the safety profiles of marketed dietary supplements to ensure the American public that these products carry minimal risk. The FDA must take swift action to remove from the market those dietary supplement products that present unnecessary risk to consumers.

The AMA offers three recommendations to CFSAN which should help achieve these goals. First, the FDA should work with the United States Pharmacopeia (USP), a not-for-profit standards-setting organization that is recognized under federal law for establishing standards for the identity, strength, quality, purity, packaging, and labeling of drugs. The USP has established similar standards for vitamin products and, currently, is establishing standards for botanicals.

The FDA should rely upon the USP to set standards for the identity, strength, quality, purity, packaging, and labeling of all dietary supplements. Furthermore, the FDA should require, or if that is not possible, strongly recommend that all dietary supplement products meet USP standards. Such products should be allowed to carry a statement that the product meets the USP's standards. Consumers should be educated regarding the importance of using dietary supplements that meet USP standards.

The AMA also recommends that the FDA develop specific GMP regulations for dietary supplements to ensure that these products are manufactured in a satisfactory manner. The FDA should undertake a strong program of plant inspections to ensure that the GMP regulations are adhered to by manufacturers and take enforcement actions as necessary.

Finally, the AMA urges the FDA to adopt a vigorous Adverse Event Reporting program for dietary supplements to identify and take necessary action when safety problems occur with marketed dietary supplement products. In 1998, the AMA's House of Delegates specifically asked the AMA "to work with the FDA to educate physicians and the public about the FDA's *MedWatch* program and to strongly encourage physicians and the public to report potential adverse events associated with dietary supplements and herbal remedies to help support FDA's efforts to create a database of

adverse event information on these forms of alternative therapies." As discussed in the enclosed AMA letter to Dr. Jane Henney, dated May 27, 1999, the AMA is an active *MedWatch* partner and would be pleased to pursue discussions with the FDA and other appropriate organizations to expand and publicize *MedWatch* as a mechanism to begin to acquire the needed safety information about dietary supplements.

In addition to *MedWatch*, the FDA also has a Special Nutritional Adverse Event Monitoring System and consumer hotline telephone numbers to obtain information about safety problems with dietary supplements. All of these programs should be integrated and enhanced to yield a systems approach to adverse event reporting for dietary supplements that is manifested by efficient management and operation and ensures that those dietary supplements with safety questions are expeditiously addressed and consumer confidence is maintained.

It has been estimated that 18% of Americans receiving prescription drugs also are taking herbal remedies and/or high-dose vitamins (see Eisenberg DM et al. *JAMA*. 1998;280:1569-1575). Does the degree of safety of dietary supplements change in individuals who have pre-existing diseases or conditions, or in those individuals who are also taking prescription medications? For example, can a dietary supplement interact with a prescription drug and result in an adverse outcome for the individual? Thus, as part of an enhanced Adverse Event Reporting program for dietary supplements, the FDA must make every effort to ensure that these types of safety problems also will be addressed.

3. To the extent possible, CFSAN must ensure that structure/function claims for dietary supplements can be substantiated by good science. When consumers ingest dietary supplement products, they should be confident that the products will perform in a manner consistent with the structure/function claims that are made in the labeling. A primary concern of the AMA with the DSHEA is the lack of a requirement for FDA premarket evaluation of the scientific data to support a structure/function claim. Therefore, the AMA urges the FDA to be especially vigilant in monitoring such claims for truthfulness. The FDA must take as aggressive an enforcement approach that the law will allow in requiring dietary supplement manufacturers to provide the necessary evidence to substantiate the structure/function claims that are being made for their products. When a structure/function claim cannot be substantiated by good science or the product makes a disease claim, the FDA must move swiftly to remove the product from the market.

In conclusion, the AMA believes the DSHEA fails to provide adequate regulatory oversight of dietary supplement products by the FDA and modifications to the current federal law are necessary. However, in the absence of modifications to the law, the AMA believes the FDA, primarily CFSAN, can undertake a regulatory strategy that will help the FDA meet its primary responsibility to protect the health of the public. As discussed above, the AMA believes that CFSAN must ensure that consumers can clearly differentiate drug products from dietary supplement products (particularly herbal remedies) so each type of product is used appropriately; that CFSAN must ensure that dietary supplements are of high quality and have a safety profile that warrants direct purchase by consumers without health professional supervision; and that CFSAN must ensure, to the extent possible, that structure/function claims for dietary supplements can be substantiated by good science.

Docket No. 99N-1174
August 19, 1999
Page 5

The AMA appreciates the opportunity to comment on this important issue and would be pleased to discuss its concerns and proposals regarding dietary supplements more fully with the FDA. Please direct any questions or comments to Margaret Garikes in our Washington Office, at 202-789-7409.

Sincerely,

A handwritten signature in cursive script, appearing to read "E. Ratcliffe Anderson, Jr.", written in dark ink.

E. Ratcliffe Anderson, Jr., MD

Enclosures

American Medical Association

Physicians dedicated to the health of America

COPY



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Executive Vice President, CEO Chicago, Illinois 60610 312 464-4184 Fax

May 27, 1999

Jane E. Henney, MD
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Henney:

In 1997, 42% of the adult population of the United States (83 million people) used at least one alternative therapy. Among the most commonly used alternative therapies were herbal remedies and megavitamins, which generally are classified as dietary supplements. Moreover, an estimated 15 million adults in 1997 took prescription medications concurrently with herbal remedies and/or high-dose vitamins (18.4% of all prescription users) (see Eisenberg DM et al. *JAMA*. 1998;280:1569-1575).

The physician members of the American Medical Association (AMA) are concerned about the quality, safety, and efficacy of dietary supplement products, especially herbal remedies. Do these products actually contain the active ingredient(s) (and strength[s]) that their manufacturers claim on the labeling? Are these products really as safe as the promotional materials of the manufacturers claim them to be? Does the degree of safety change in individuals who have pre-existing diseases and conditions, or in those individuals who are also taking prescription medications? Are the structure/function claims for these products accurate and based on good science? Are these products being used inappropriately to treat diseases or potentially delaying individuals with diseases from obtaining effective prescription medications? Satisfactory answers to these questions appear to be unavailable.

The AMA believes that the primary problem is the Dietary Supplement Health and Education Act of 1994 (DSHEA), which failed to provide for adequate regulatory oversight of these dietary supplement products by the Food and Drug Administration (FDA). In that regard, our House of Delegates has asked the AMA to work with Congress to modify the DSHEA to require that dietary supplements and herbal remedies, including those products already in the marketplace, undergo FDA approval for evidence of safety and efficacy; meet standards established by the United States Pharmacopeia (USP) for identity, strength, quality, purity, packaging, and labeling; and meet FDA postmarketing requirements to report adverse events, including drug interactions.

Recognizing that changing the federal law may be difficult to achieve at this time, our House of Delegates also asked "that the AMA work with the FDA to educate physicians and the public about the FDA's *MedWatch* program and to strongly encourage physicians and the public to report potential adverse events associated with dietary supplements and herbal remedies to help support FDA's efforts to create a database of adverse event information on these forms of alternative therapies."

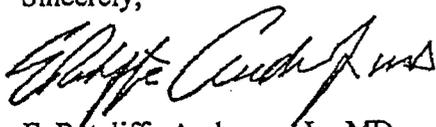
Jane E. Henney, MD
May 27, 1999
Page 2

The AMA has been an active *MedWatch* partner since the inception of this adverse event reporting program. We believe that *MedWatch* has achieved its goal of providing appropriate signals for adverse events associated with drugs and devices. Expanding *MedWatch* to include reporting potential adverse events associated with dietary supplements seems to be a reasonable approach to begin the collection of necessary adverse event information on these products. In particular, if 18% of Americans receiving prescription drugs also are taking herbal remedies and/or high-dose vitamins, signals for potential adverse interactions between prescription medications and dietary supplements would likely be reported.

The AMA would be interested in obtaining the views of the FDA on this subject. If the perceived need for adverse event information on dietary supplements is mutual, the AMA would be pleased to pursue discussions with the FDA and other appropriate organizations to expand and publicize *MedWatch* as a mechanism to begin to acquire the needed information.

The AMA appreciates your attention to this matter.

Sincerely,

A handwritten signature in black ink, appearing to read "E. Ratcliffe Anderson, Jr., MD". The signature is written in a cursive, flowing style.

E. Ratcliffe Anderson, Jr., MD

American Medical Association

Physicians dedicated to the health of America



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August 4, 1999

Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

RE: Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Products on the Structure or Function of the Body [Docket No. 98N-0044]

On August 26, 1998, the American Medical Association (AMA), which represents approximately 300,000 physicians and physicians-in-training, provided written comments to the Food and Drug Administration (FDA) regarding the Proposed Rule entitled, "Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Products on the Structure or Function of the Body," 63 Fed. Reg. 82, pp. 23624-23632 (April 29, 1998). A copy of the AMA's comments is enclosed.

Recently, the FDA published a Notice that it was reopening the comment period on this Proposed Rule, 64 Fed. Reg. 130, pp. 36824-36826 (July 8, 1999). Specifically, the FDA is requesting further comment on three issues: 1) definition of disease; 2) common conditions associated with natural states; and 3) implied disease claims. The purpose of this follow-up letter is to present the AMA's views on these issues.

In its original letter to this Docket and in a subsequent letter to FDA Commissioner Jane E. Henney, MD (also enclosed), the AMA has expressed its profound concern regarding the lack of FDA's authority to adequately regulate dietary supplements to ensure their safe and appropriate use and to protect the health of the public. The AMA recognizes that the primary problem is the Dietary Supplement Health and Education Act of 1994 (DSHEA), which failed to provide for adequate regulatory oversight of these dietary supplement products by the FDA. In that regard, the AMA's House of Delegates has asked the AMA to work with Congress to modify the DSHEA to require that dietary supplements and herbal remedies, including those products already in the marketplace, undergo FDA approval for evidence of safety and efficacy; meet standards established by the United States Pharmacopeia (USP) for identity, strength, quality, purity, packaging, and labeling; and meet FDA postmarketing requirements to report adverse events, including drug interactions.

In the absence of modifications to current federal law, the AMA believes the FDA has the responsibility to do its utmost to protect the health of the public by regulating dietary supplements to the greatest extent possible. **Thus, the AMA is deeply troubled by the possibility that the FDA may lower its proposed regulatory standards on "structure/function claims" that can be made by manufacturers of dietary supplements. If the FDA does not hold firm to its proposed regulations, as described in the Federal Register of April 29, 1998, the Agency will further blur the distinction between a drug and a dietary supplement (in particular "herbal remedies") and elevate the level of confusion among consumers regarding appropriate therapies. Such an action by the FDA clearly would be in conflict with its mission to protect the health of the public.**

Definition of Disease

In its earlier letter to this Docket, the AMA supported FDA's definition of a disease, as proposed under Sec. 101.93(g)(1) of the April 29, 1998 Proposed Rule. However, the AMA recommended that the definition could be improved and made more complete by adding the phrase, "or a state of health leading to such deviation, impairment, or interruption," i.e., proposed Sec. 101.93(g)(1) would be comparable to the FDA's proposed amendment of Sec. 101.14(a)(6). The AMA's rationale for this additional phrase was to include individuals with a "state of health" that puts them at increased risk for full-blown disease. The examples we gave were individuals who are overweight or who have elevated cholesterol levels and who would be at increased risk of heart disease. Inclusion of these abnormal "states of health" within the definition of disease would be consistent with FDA's very appropriate determination that terms such as "obesity" and "hypercholesterolemia" are diseases, and only drugs can carry claims for their treatment.

The AMA opposes any narrowing of the definition of a disease from the above recommendation. It is imperative that individuals with "any deviation from, impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms (including laboratory or clinical measurements that are characteristic of a disease), or a state of health leading to such deviation, impairment, or interruption" be recognized as having a disease. Thus, such individuals can benefit from drug products with a known benefit/risk ratio based on rigorous scientific study and regulatory review, rather than be confused by dietary supplement claims that are based on far less scientific rigor.

Common Conditions Associated With Natural States

The AMA is fully supportive of proposed Sec. 101.93(g)(2)(iii) and of FDA's interpretation of that section, as discussed on p. 23627 of the April 29, 1998 Proposed Rule. Specifically, the AMA agrees with the FDA's view that "a consequence of a natural state that presents a characteristic set of signs or symptoms that are recognizable to health care professionals or consumers as constituting an abnormality of the body" should be considered a disease claim. This should be the case regardless of whether the abnormality is life threatening (e.g., Alzheimer's disease associated with aging) or is a set of unpleasant symptoms that will subside regardless of therapeutic intervention (e.g., premenstrual syndrome associated with the menstrual cycle in some women).

For many common conditions associated with natural states, drug products are already available or likely will become available with advancements in science. As noted in the preceding section, drug products have well known benefit/risk ratios based on rigorous scientific study and regulatory review. From the AMA's perspective, it would be unwise and confusing to allow dietary supplement products to contain similar claims because the evidence to support the claim is not subject to pre-market regulatory review. Moreover, the incentives to manufacturers to pursue new drug approvals would be substantially diminished if there was reason to believe that a product could be marketed as a dietary supplement for the same claim.

Implied Disease Claims

The AMA strongly supports the views expressed by the FDA on pp. 23626-23627 and in proposed Sec. 101.93(g)(2) of its April 29, 1998 Proposed Rule that a statement that implicitly claims an effect on a specific disease or class of diseases should be classified as a disease claim. To do otherwise would make

a mockery of the important distinction between drug products and dietary supplement products. To argue that "for the treatment of lung cancer" is a disease claim, but that "shrinks tumors of the lung" should be a structure/function claim is absurd. Any reasonable consumer or physician would not see a difference between these two statements. However, there is a marked difference in the level of evidence that must be reviewed by the FDA to approve a drug for a disease claim versus what is needed to make a structure/function claim for a dietary supplement.

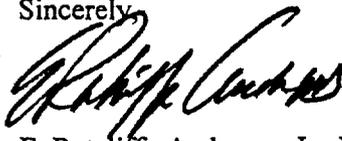
To allow implied disease claims to be made for dietary supplements is dangerous for individuals with diseases because they may elect to use a dietary supplement in lieu of obtaining a diagnosis and appropriate drug treatment from a physician. In the above example, such a scenario could result in death. It is the AMA's view that if the FDA were to allow dietary supplements to make implied disease claims, it would substantially undermine the current drug approval process in the United States, and the FDA's ability to protect the health of the public would be substantially diminished.

In its earlier letter, the AMA argued that even if the FDA's efforts to differentiate structure/function claims from disease claims as promulgated in the April 29, 1998 Proposed Rule become finalized, there are still concerns. The AMA pointed out that some of the structure/function claims that the FDA considered acceptable are debatable. For example, "inhibits platelet aggregation" could be considered an implied disease claim for "prevents heart attacks," "improves absentmindedness" could be considered an implied disease claim for "Alzheimer's disease," and "support for the immune system" could be considered an implied disease claim for "treatment for human immunodeficiency virus (HIV) infection." Thus, despite the FDA's best efforts, the AMA remains unconvinced that the health of the public would be adequately protected by the April 29, 1998 Proposed Rule. To lower the standards further would be unconscionable.

In conclusion, the AMA remains supportive of the FDA's April 29, 1998 Proposed Rule. We hope that finalizing this Rule unaltered, except for the AMA's recommended change in the definition of disease as noted above, will significantly diminish inappropriate "disease claims" on dietary supplement labels. **The AMA vigorously opposes the lowering of FDA's proposed regulatory standards on "structure/function claims" that can be made by manufacturers of dietary supplements, as discussed in the July 8, 1999 Federal Register Notice. Narrowing the definition of disease and/or allowing dietary supplements to make implied disease claims or claims for abnormal conditions associated with natural states will further blur the distinction between a drug and a dietary supplement, increase confusion among consumers regarding appropriate therapies, and diminish the FDA's ability to protect the health of the public. The AMA urges the FDA to hold firm to its Proposed Rule of April 29, 1998.**

The AMA appreciates the opportunity to comment on this important issue and would be pleased to discuss its concerns regarding dietary supplements more fully with the FDA. Please direct any questions or comments to Margaret Garikes in our Washington Office, at 202-789-7409.

Sincerely,



E. Ratcliffe Anderson, Jr., MD

Enclosures

American Medical Association

Physicians dedicated to the health of America



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August 26, 1998

Dockets Management Branch
(HFA-305)
Food and Drug Administration
12420 Parklawn Drive
Room 1-23
Rockville, Maryland 20857

RE: Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body [Docket No. 98N-0044]

Dear Sir or Madame:

The American Medical Association (AMA), representing approximately 300,000 physicians and physicians-in-training, is pleased to comment on the Food and Drug Administration's (FDA) Proposed Rule entitled, "Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body." 63 Fed. Reg. 82, pp. 23624-23632 (April 29, 1998). This Proposed Rule is intended to define the types of statements that can be made by a manufacturer concerning the effect of a dietary supplement on the structure and function of the body. Such claims are allowed under the Dietary Supplement Health and Education Act of 1994 (DSHEA). In addition, the proposed regulations also establish criteria for determining when a statement about a dietary supplement is a claim to diagnose, cure, mitigate, treat, or prevent disease. Such claims are prohibited under the DSHEA.

The AMA supports the definition of a disease, as proposed under 101.93(g)(1), but we believe it would be improved and made more complete by adding the phrase "or a state of health leading to such deviation, impairment, or interruption." For example, individuals who are overweight or have elevated cholesterol levels could be considered to have a "state of health" that puts them at an increased risk for heart disease. Yet the FDA appropriately considers obesity or hypercholesterolemia as diseases, and only drugs can carry claims for their treatment.

The AMA supports the FDA's efforts to differentiate "structure/function claims" from "disease claims" to provide guidance on what claims will be permitted for dietary supplements under the DSHEA. The detailed criteria for identifying disease claims, as discussed in the Proposed Rule [101.93(g)(2)(i-x) and the accompanying introduction on pp.23626-23628], will to some degree clarify what "structure/function claims" can be made for dietary supplements and, more important, significantly diminish the number of inappropriate "disease claims" for these types of products.

The task faced by the FDA in developing the criteria for identifying disease claims is complex and difficult; we believe that some of the "structure/function claims" that the FDA considers acceptable are debatable. For example, "inhibits platelet aggregation" could easily be construed to mean, "prevents heart attacks." Similarly, "improves absentmindedness" could be misinterpreted as a therapy for Alzheimer's disease. Individuals infected with the human immunodeficiency virus (HIV) may believe that a dietary supplement that claims to "support the immune system" is a therapy for their disease. Thus, despite the FDA's best efforts, the AMA is not convinced that the health of the public will be adequately protected by this Proposed Rule.

Dockets Management Branch
August 26, 1998

The fundamental problem lies with the DSHEA itself. By allowing dietary supplement manufacturers to make "structure/function claims" without FDA's pre-approval based on credible scientific evidence of safety and efficacy, the public must rely on the manufacturer's good faith assertion that they can substantiate their claim. This is in contrast to drugs where FDA pre-approval of efficacy claims is necessary for marketing the product. Furthermore, some types of dietary supplements, such as botanicals, are not well characterized chemically. Thus, the AMA is concerned that the FDA lacks sufficient statutory and regulatory authority to adequately regulate dietary supplements to ensure their safe and appropriate use.

An additional concern that is not addressed in the Proposed Rule is whether manufacturers can be required to report adverse events associated with dietary supplements to the FDA and to include this information in the labeling. For example, if a manufacturer of a dietary supplement claims that the product "inhibits platelet aggregation," would it be required to report cases of excessive bleeding? Would it be required to report a drug interaction, for example, with the commonly prescribed anticoagulant warfarin? Because little is known about the pharmacology of many dietary supplements, potential risks in individuals with underlying diseases and/or those taking traditional drugs are largely unknown. Again, the AMA raises the concern that the FDA lacks the regulatory authority to require this important safety information to be included in the labeling of dietary supplements when it is known.

In conclusion, the AMA commends the FDA for this Proposed Rule that we hope will significantly diminish inappropriate "disease claims" on dietary supplement labels. However, the AMA remains deeply concerned that the FDA's regulatory authority over dietary supplements is insufficient to adequately protect the health of the public. The AMA appreciates the opportunity to comment on this important Proposed Rule and would be pleased to discuss its concerns regarding dietary supplements more fully with the FDA. Please direct any questions or comments to Margaret Garikes in our Washington Office, at 202-789-7409.

Sincerely,



E. Ratcliffe Anderson, Jr., MD

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