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April 3, 2003

VIA FEDERAL EXPRESS

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

Re: Request for Comments on Dietary Supplements Containing Ephedrine Alkaloids (68 Fed. Reg. 10417, March 5, 2003)

Docket No. 95N-0304

Dear Sir or Madam:

These comments are being submitted on behalf of Metagenics, Inc. ("Metagenics") of San Clemente, California, pursuant to the FDA's "Dietary Supplements Containing Ephedrine Alkaloids: Reopening of the Comment Period " published in the Federal Register of March 5, 2003.[1] Metagenics is a manufacturer and supplier of high quality dietary supplements providing numerous health benefits for consumers. The Company markets its products under its own name, as well as under the Ethical Nutrients, Unipro, and MetaBotanica brand names.

Metagenics does not currently sell or manufacture dietary supplements containing ephedrine alkaloids (i.e. ephedra). However, as a member of the dietary supplement industry, Metagenics feels compelled to respond to FDA's reopening of the comment period for the proposed rule on dietary supplements containing ephedrine alkaloids, originally published in the Federal Register of June 4, 1997.[2]

Metagenics respectfully submits that FDA's request for comments on "what additional legislative authorities, if any, would be necessary or appropriate to enable FDA to address this issue most effectively" is disingenuous and misleading. Metagenics is perplexed by FDA's insinuation that the agency needs additional legislative authority to effectively regulate dietary

[1] See 68 Fed. Reg. 10417. 95N-0304 C 3873

[2] See 62 Fed. Reg. 30678.

supplements containing ephedrine alkaloids (or any other dietary supplement). The regulatory authority afforded FDA under the Federal Food, Drug and Cosmetic Act (FDCA) as well as the Dietary Supplement Health and Education Act of 1994 (DSHEA) includes a broad range of enforcement powers such as seizure, condemnation, and destruction, as well as the outright removal of products from the market. Furthermore, FDA currently regulates the types of ingredients that can be used in dietary supplements, the purity of those ingredients, and the types of claims that can be made on behalf of the products themselves. What additional powers does FDA believe are necessary to allow it to protect the public health? Metagenics submits that FDA needs no additional powers to fulfill this mission, and that its failure to enforce the law as it is currently written constitutes a complete abdication of its responsibilities to the public health.

Metagenics believes that FDA's request for additional powers to regulate dietary supplements is arbitrary and capricious. Metagenics is also very concerned about FDA's continued misrepresentation of the scientific evidence on ephedra to the public and the media. FDA's longstanding position against ephedra products, in spite of the weight of positive clinical research, makes evident that FDA's ultimate goal is to ban all ephedra products. However, FDA's numerous efforts to restrict the sale of ephedra supplements over the past several years have repeatedly been defeated because the agency has never been able to establish that these products are ineffective and/or unsafe when used as directed. If FDA believes it cannot regulate ephedra products in the manner it desires, it is only because the scientific literature indicates that these products are in fact safe and effective *when used as directed pursuant to industry standards*. It is not because FDA lacks regulatory authority.

Given FDA's history of bias against the dietary supplement industry, and especially against ephedra products, Metagenics respectfully submits that any additional enforcement powers granted to FDA would likely result in the improper and excessive regulation of ephedra products, as well as other dietary supplements, by the agency, to the detriment of the industry and consumers.

I. FDA ENFORCEMENT POWERS UNDER THE FEDERAL FOOD, DRUG AND COSMETIC ACT (FDCA) AND THE DIETARY SUPPLEMENT HEALTH AND EDUCATION ACT (DSHEA) OF 1994

1. The Federal, Food, Drug and Cosmetic Act (FDCA)

Under the FDCA, it is illegal to market any food, drug, device, or cosmetic that is adulterated or misbranded.[3] A food is adulterated if it "bears or contains any poisonous or deleterious substance which may render it injurious to health."[4] A product is misbranded if,

[3] See 21 U.S.C. 331.

[4] See 21 U.S.C. 342(A)(1).

among other things, its labeling is false or misleading.[5] Under these fundamental principles of Food and Drug law, a product is marketed illegally if its label includes misrepresentations concerning its contents, the safety or efficacy of those contents, or if there is anything in the product that is not supposed to be there. This is true whether the product is a conventional food or a dietary supplement.

With respect to enforcement, the FDCA expressly allows federal courts to enjoin violations of the Food and Drug laws and allows the seizure of any misbranded or adulterated food, drug or cosmetic or device by the FDA.[6] Moreover, FDA has sole discretion to bring enforcement actions for such violations, which are punishable civilly and criminally. Section 303 of the FDCA states that any person who commits a prohibited act shall be imprisoned for not more than one year or fined not more than $1,000. Violations with intent to defraud or mislead are punishable by up to three years imprisonment, a $10,000 fine, or both.

In addition, FDA has the authority to conduct inspections in order to determine whether any violations of the Food and Drug laws are taking place.[7] FDA may inspect "at reasonable times" and in "reasonable manner," any "establishment" as well as "finished and unfinished materials, containers and labeling" connected with the manufacture or marketing of dietary supplements.

None of these powers have been abridged by the Dietary Supplement Health and Education Act of 1994 (DSHEA) or any other federal law. FDA still has full regulatory authority to bring enforcement actions for violations of the Food and Drug laws. FDA can only blame itself if such actions are not brought.

2. The Dietary Supplement Health and Education Act of 1994 (DSHEA)

Since the passage of the Dietary Supplement Health and Education Act (DSHEA) in 1994, FDA has taken the public position that it is prevented from taking effective regulatory action against illegal dietary supplements (i.e. products that are unsafe or make false or misleading claims). In a 1995 press release following the passage of DSHEA, FDA stated that "dietary ingredients used in dietary supplements are no longer subject to the premarket safety evaluations required of other new food ingredients or for new uses of old good ingredients."[8]

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[5] See 21 U.S.C. 343.

[6] See 21 U.S.C. 332, 334.

[7] See 21 U.S.C. 374.

[8] Dietary Supplement Health and Education Act of 1994, FDA Press Release (December 1, 1995).

FDA also alluded to the fact that DSHEA had somehow stripped FDA of its ability to ensure the safety of dietary supplements. Other FDA press releases and public statements following the passage of DSHEA referred to the regulation of dietary supplements as a "post-marketing program."[9] In reality, however, DSHEA expanded agency regulation of supplements in a number of ways.

In addition to the previously existing provisions of the FDCA, DSHEA provides that a dietary supplement is adulterated if it "presents a significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling," or under ordinary conditions of use. Furthermore, a "new dietary ingredient" must provide reasonable assurances that it does not pose an imminent hazard to public health or safety." A new dietary ingredient will be deemed adulterated unless it has been present in the American food supply since October 15, 1994 or can establish a history of use or other evidence of safety.[10] The use of a new dietary ingredient must be notified to FDA at least 75 days before it is placed on the market. Therefore, with respect to new dietary ingredients, FDA has the power to restrict and deny access to the marketplace.

DSHEA also requires companies to possess substantiation prior to the making of any structure/function claim.[11] Under this standard, the threshold issue in any claims-based FDA enforcement action is no longer whether the claim is true but whether the company making the claim actually possessed substantiation at the time the claim was made.

As the above examples illustrate, DSHEA has done nothing to strip FDA of its enforcement powers against the illegal marketing of dietary supplements. In fact, DSHEA has expanded FDA's ability to remove products from the shelf. DSHEA expressly allows FDA to immediately remove a dietary supplement from the marketplace upon a finding by the Secretary of Health and Human Services that it poses an imminent hazard to public health.[12] Once the product is removed, FDA then has the burden of proving that it presents a significant or unreasonable risk of injury when used as indicated on the product label.

In short, DSHEA provides that a dietary supplement that is adulterated or misbranded or that bears an unauthorized drug claim is subject to seizure, condemnation or destruction and may

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[9] Statement by Joseph A. Levitt, Esq., Director, Center for Food Safety and Applied Nutrition, FDA, Before the Comm. on Gvt. Reform, Chairman Dan Burton, U.S. House of Representatives (March 20, 2001).

[10] See 21 U.S.C. 413.

[11] See 21 U.S.C. 343(r)(1)(b).

[12] See 21 U.S.C. 342.

be taken off the shelves by FDA. It should be noted that DSHEA also granted FDA the authority to establish good manufacturing practices to govern the preparation, packing, and holding of dietary supplements to ensure safety. FDA just recently published a proposed rule for good manufacturing practices for dietary supplements.[13] Once a final rule is adopted, FDA will have even more direct control over dietary supplements before they reach the market.

II HISTORY OF FDA'S BATTLE AGAINST EPHEDRA PRODUCTS:

1. The 1997 Proposed Rules

FDA's motives regarding ephedra supplements were revealed in1997 when the agency published a proposed rule for dietary supplements containing ephedrine alkaloids, which would have rendered these products useless for their intended purpose, namely, weight loss. The proposal was highly controversial and caused the industry to question FDA's basis for the proposed restrictions. As FDA's proposal drew more and more criticism from the industry, the House Committee on Science requested that the Government Accounting Office (GAO) conduct a review of FDA's scientific basis as well as the agency's cost/benefit analysis of the proposed rule. The 1999 80-page GAO report entitled "Dietary Supplements: uncertainties in Analyses Underlying FDA's Proposed Rule on Ephedrine Alkaloids" confirmed that FDA did not possess any scientific basis for its proposed restrictions on ephedra products. Remarkably, FDA had not even attempted to establish causality between ephedra consumption and the Adverse Event Reports (AERs) the agency used as the basis for the proposed regulations.

Among other things, the 1997 proposal sought to prohibit the combination of ephedra with stimulants such as caffeine and prohibited the making of weight loss claims. However, FDA inexplicably rejected successful clinical studies showing that ephedrine was useful in weight loss. After it was formally revealed that FDA did not possess any scientific basis to support its restrictions on ephedrine products, FDA was forced to withdraw significant portions of its proposed rule. On April 3, 2000, FDA withdrew the proposed restrictions concerning potency, labeling claims, and directions for use.[14]

2. The 2003 Proposed Warnings for Dietary Supplements Containing Ephedrine Alkaloids:

On February 28, 2003, FDA reopened the comment period for the 1997 proposed rule on dietary supplements containing ephedrine alkaloids, proposed new warnings for these products, and issued nearly thirty warning letters against ephedra products making unsubstantiated claims about sports performance enhancement.

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[13] See 68 Fed. Reg. 12158.

[14] See 54 Fed. Reg. 17474.

FDA's current proposal does not include formulation restrictions. FDA appears to have abandoned the idea of restricting the combination of ephedrine alkaloids with other stimulants such as caffeine.[15] However, the proposed warnings include a mandatory front panel warning statement in boldface that "heart attack, stroke, seizure, and death have been reported after consumption of ephedrine alkaloids." This statement is simply not supported by the scientific literature, including the "Rand Report," which FDA used as a basis for its new proposal.

Metagenics is very concerned about FDA's continued misrepresentation of the scientific literature with respect to the safety and efficacy of ephedra. Even more troubling is the agency's apparent disregard for the need for science-based regulations. The same day FDA reopened the comment period for the 1997 proposed rule, FDA released the "Rand Report," which was commissioned by the National Institute of Health to review evidence on the risks and benefits of ephedra and ephedrine in weight loss and athletic performance. Although the Rand Report expressly stated that the short-term use of ephedra (with and without caffeine) was associated with a "statistically significant" increase in weight loss compared to placebo, FDA's press release stated that Rand found "limited evidence of an effect of ephedra on short-term weight loss." Even more significant was the Rand finding that no serious adverse events were reported in the 52 clinical trials of ephedra supplements that were analyzed for safety. Yet, FDA's press release stated that ephedra, as currently marketed, may be associated with unreasonable safety risks. It appears FDA continues to denigrate ephedra in an effort to undermine DSHEA.

As a reputable manufacturer of legitimate dietary supplements, Metagenics is astounded that FDA would utterly abandon a careful scientific approach to regulation products within its jurisdiction. Given these circumstances, it would be pointless to provide FDA with any additional legislative authority, when the agency already has all the necessary enforcement powers at its disposal to ensure that all dietary supplements are safe. There is nothing stopping FDA from pulling ephedra products off the shelves tomorrow, except for the wealth of scientific literature that supports its safety and efficacy when used as directed, including FDA's own independent study conducted by the Rand Corporation.

CONCLUSION

Metagenics supports the responsible marketing of dietary supplements and the use of science-based warnings. In the case of ephedra products, Metagenics supports the industry standards established by the American Herbal Products Association (AHPA) which include limits on daily doses, restrictions against marketing ephedra for herbal "highs," require mandatory warnings, and prohibit the sale of ephedra to minors. These initiatives, which have been voluntarily adopted by industry members, indicate that the industry is committed to the responsible marketing of ephedra products. More importantly, the industry is aware of the potential dangers associated with the abuse and/or misuse of ephedra and has already taken the

[15] See 62 Fed. Reg. 30678.

appropriate measures to protect the public health.

Metagenics respectfully submits that FDA could better serve the public by working alongside industry organizations such as AHPA and developing scientific regulations for ephedra products. Metagenics does not believe that the recent warnings proposed by FDA are supported by the scientific literature or the Rand Report. Adopting such unsubstantiated regulations for ephedra products not only sets unsound precedent for the regulation of dietary supplements but also fails to serve the pubic health. Finally, Metagenics does not believe that FDA needs any new legislative authority to effectively regulate dietary supplements.

Respectfully submitted,

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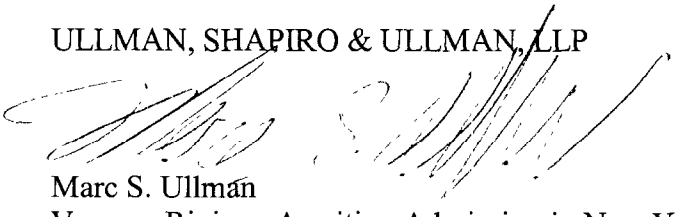

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