



Pennsylvania  
MEDICAL SOCIETY<sup>®</sup>

March 27, 2003

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

**Re: Dietary Supplements Containing Ephedrine [Docket No. 95N-0304]**

The Pennsylvania Medical Society has reviewed the comments of the the American Medical Association (AMA) to this Docket on the health risks associated with dietary supplements containing ephedrine (ephedra) alkaloids. We support the scientific arguments expressed in the AMA's letter and call for a ban on dietary supplements containing ephedrine alkaloids. We also support aggressive regulation of all dietary supplements by the Food and Drug Administration (FDA).

The Pennsylvania Medical Society believes that physicians must do whatever they can to protect the health of their patients. It is particularly vital that we prohibit the marketing of dietary supplements to the public that are not safe, especially when companies promote these products as safe, effective and "all natural" without providing any proof for their claims. With the multitude of dietary supplement products being marketed today, it is impossible for laypersons to determine if these products are safe and really work as advertised. The FDA must accept the responsibility to assure that dietary supplements are safe and provide some benefit to consumers.

We reviewed the documentation of problems with dietary supplements containing ephedra alkaloids cited in the AMA's letter and believe they are extremely convincing. In particular:

- The FDA has received more than 18,000 Adverse Event Reports associated with ephedra-containing dietary supplement products, and Bent et al found that, based on reports to Poison Control Centers, the relative risk observed for ephedra-containing herbal products was more than 100-fold greater than for any other herb (a finding that is difficult to explain by reporting bias alone).
- Independent reviewers, such as Shekelle et al, Haller and Benowitz, and others, have concluded that a number of serious adverse events, including deaths, are definitely or probably caused by ephedra because no other plausible explanation exists.
- The RAND study (Shekelle et al) found that the benefits of ephedra-containing dietary supplements are minimal; only very modest benefit for short-term weight loss was observed and, at the dosages used, subjects experienced substantial psychiatric, autonomic, gastrointestinal, and cardiac side effects.

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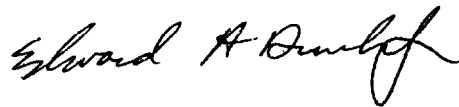
Because ephedra alkaloids are considered food supplements, are available to all Americans, and have very limited regulation, these products should be safer than drug products and have a very high benefit to risk ratio when compared to drugs. Unfortunately, the available scientific evidence suggests that the risks of ephedra *far* outweigh the benefits and Americans who ingest these products are being placed at significant risk.

The Pennsylvania Medical Society firmly believes that dietary supplement manufacturers should bear the burden to prove that claims of efficacy and safety for their products are accurate. For far too long, these products have escaped adequate FDA regulation by being labeled as dietary supplements instead of drugs. However, until one can secure a change in the Dietary Supplement Health and Education Act of 1994 (DSHEA), the FDA must do whatever it can to assure that existing mechanisms for regulation are used to the fullest extent possible.

The Pennsylvania Medical Society strongly concurs with the AMA that a benefit/risk calculus should be sufficient for the FDA to determine if dietary supplements containing ephedra alkaloids, or any other dietary supplement products, present a “significant or unreasonable risk of illness or injury.” Requiring the FDA to prove – prospectively and unequivocally - that a dietary supplement is not safe is an unreasonable standard and is unacceptable. Given the flood of these products into the market, it is impossible for the FDA to incur the expense of research into their safety and efficacy.

In the case of dietary supplements containing ephedra alkaloids, the benefit to risk ratio is clearly unacceptable. Such products show marginal benefit for short-term weight loss, but have considerable side effects, and there are many adverse event reports linking these products to deaths or serious morbidity. Given that ephedra-containing dietary supplements are classified as food supplements and are subject to virtually no regulation prior to marketing, American citizens have the right to expect that these products are extremely safe and have some benefits. Since this is not the case for dietary supplement products containing ephedra alkaloids, these products should be banned in the United States because they pose an “unreasonable risk.”

Sincerely,

A handwritten signature in cursive script, reading "Edward H. Dench".

Edward H. Dench, MD  
President