



## **Council for Responsible Nutrition**

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October 11, 2002

The Honorable Richard Durbin  
Subcommittee on Oversight of Government Management,  
Restructuring and the District of Columbia  
Government Affairs Committee  
United States Senate  
439 Hart Senate Office Building  
Washington, D.C. 20510

Dear Senator Durbin:

At this week's hearings on ephedra-containing dietary supplements, HHS Secretary Tommy Thompson called on FDA to require strong warnings on such products. The members of the Council for Responsible Nutrition (CRN) and the dietary supplement industry as a whole have already adopted such warnings, and we are anxious to explore other ways of educating consumers about the appropriate use of these products. We also fully support continuing FDA efforts to eradicate inappropriate uses of dietary supplements (such as their marketing as "street drugs") and to prohibit the inclusion of pharmaceutical ingredients in supplements.

Ephedra is clearly not for everyone, but has been shown in the marketplace as well as in clinical trials to provide effective and meaningful support for weight loss for many people. This is highly relevant today, in the midst of a recognized epidemic of obesity in this country and in view of the difficulty experienced by many people in achieving weight loss. Dr. George Bray, one of the country's leading experts on the health risks of obesity, testified to this effect at your July 31 hearing on ephedra-containing supplements.

All of the dietary supplement associations have long recommended strong warnings for ephedra-containing products, and these have been adopted by virtually all manufacturers. Indeed, the associations petitioned FDA in 2000 to finalize a regulation requiring such a warning. The warning currently recommended is similar to the one proposed by FDA in 1997 and is also similar to those required by some state laws. Attached is a copy of the label warning recommended by CRN to its member companies. It is difficult to conceive that a stronger warning could possibly be crafted.

The prominence of the label warning is an issue that was also addressed at this week's hearing. All of the trade associations recognize and recommend that the warning should

be prominent and conspicuous, and it generally appears in bold type. However, because of its length, the warning can occupy an entire label panel on a small or even a medium-sized container, and readability may not be optimal. It may be desirable for the industry to explore other alternatives, such as the addition of a shelf warning, to help bring the necessary cautions to the attention of consumers.

FDA noted at the hearing that recent enforcement actions have been taken against ephedra-containing products being marketed as “street drugs,” including one called “Yellow Jackets.” Enforcement action in this area has been actively supported by CRN and other industry associations ever since such products emerged in the early 1990s, but action by FDA or FTC has been minimal. Thus, the illegitimate marketing of “street drug alternatives” masquerading as dietary supplements has continued, despite FDA’s 2000 policy statement clearly indicating that such products would be viewed as illegal.

FDA has taken action against some products containing synthetic ephedrine instead of or in addition to herbal ephedra. The dietary supplement industry has long supported the proposition that the addition of synthetic ephedrine to any supplement product is illegal, and we applaud the agency’s initiatives to ensure that the requirements of the law are met.

Another focus of the hearing was the analysis of adverse event reports provided by Metabolife, the largest marketer of ephedra-containing dietary supplements intended for use in weight loss. These reports are similar to those collected by FDA over the past decade, in that they provide a useful signal indicating the need for more in-depth evaluation, but by themselves are not reliable indicators of a causal effect. Nor do they provide sufficient information to define a Lowest Observed Adverse Effect Level (LOAEL) or a No Observed Adverse Effect Level (NOAEL). It was this inadequacy that led the Government Accounting Office to conclude in 1999 that FDA lacked sufficient support for the particular dosage limit the agency proposed in 1997. Thus, other types of analysis are necessary in order to help define a safe intake level. There is currently no requirement to submit adverse event reports to FDA for dietary supplements, conventional food products, medical foods, or most over-the-counter drugs. While this may be the time to reconsider existing policy regarding mandatory reporting, CRN believes that discussion should rightfully apply to all ingestible products (foods and pharmaceuticals) currently exempt from such reporting.

Alternatively, Congress and FDA could consider a narrowly targeted requirement for a post-market surveillance system relating only to ephedra. This would be consistent with CRN policy on ephedra and also with previous FDA approaches to specific ingredients of potential concern, including aspartame and olestra. If such a targeted approach were to be adopted, it would be important that adverse event reports be analyzed in a timely and open manner, in accordance with recognized principles for evaluating causality.

CRN contracted with Cantox Health Sciences International, an internationally recognized toxicology firm, to prepare a quantitative risk assessment of ephedra-containing dietary supplements. This report concluded in 2000 that the adverse event reports do not offer

useful information for the purpose of defining a safe level of intake, when evaluated against the six recognized criteria for assessing causality. However, Cantox concluded that clinical trials and laboratory investigations do provide a sound basis for identifying a safe upper limit for ephedra. That safe upper limit is identified in the Cantox report as a quantity of ephedra providing no more than 30 mg of naturally-occurring ephedrine alkaloids per serving, to be taken no more than 3 times per day, for a maximum period of 6 months. In addition, Cantox identified the need for labeling that would warn against any use of these products by certain population groups (including children under 18) or by people with certain medical conditions (such as high blood pressure) or by persons using certain medications (such as those containing MAO inhibitors). These considerations were taken into account by CRN in developing the specific warning language now recommended for use by our member companies who manufacture or market ephedra-containing dietary supplements. (A copy of the Cantox report is available at <http://www.crnusa.org/CRNCantoxreportindex.html> on the CRN website.)

The HHS public meeting in August 2000 evaluated the information available on the safety and benefits of ephedra and recommended appropriate warnings and label indications, more consumer education, and more research. After that meeting, the NIH Office of Dietary Supplements contracted with the Rand Corporation for a systematic review of ephedra safety and benefits, and that report should provide additional information to guide FDA actions.

CRN does not believe banning ephedra is the appropriate response to the current evidence regarding this ingredient. We do believe there are at least three actions that could and should be taken to respond to the concerns expressed by you and by other legislators:

1. FDA should immediately propose a comprehensive mandatory warning statement incorporating strong language similar to that proposed by FDA in 1997, currently required by many states, and already adopted by most manufacturers of ephedra-containing products. Consideration might also be given to additional consumer education about ephedra and to the use of shelf warnings to complement or emphasize the label warnings.
2. Congress and FDA should consider establishing a post-market surveillance system for ephedra-containing products, similar to the ones previously established for other ingredients presenting potential concerns, including aspartame and olestra. Reporting and evaluation of adverse events should be timely and open, and reports should be evaluated on the basis of recognized principles for assessing causality.
3. FDA should continue and accelerate enforcement activities against dietary supplement products containing synthetic ephedrine (a drug ingredient) and against products intended for use as “street drug” alternatives.

In the meanwhile, it should be recalled that ephedra represents only a single product within the larger scope of dietary supplements. By far the largest product category is still vitamins and minerals, about which there is ample scientific information regarding both safety and benefit. Health authorities are increasingly recommending responsible longterm use of nutritional supplements for health promotion and disease prevention, and **we believe it is critical that concerns specifically related to ephedra not be used as a lever to undermine the category as a whole.**

Senator Durbin, CRN stands ready to work with you and other legislators, as well as FDA, FTC, HHS Secretary Thompson, the AMA, consumer groups, and all other parties in evaluating and developing appropriate legislation, regulations, or other actions that will help protect the public health. At the same time, it is relevant that these products are valued by millions of consumers as an aid to weight loss and have been demonstrated in clinical trials to be safe and effective when used appropriately for this purpose. CRN is convinced ephedra-containing products can be effectively regulated under the provisions of DSHEA, when the law is properly implemented and enforced.

By this letter, we request an opportunity to meet with you and the appropriate members of your staff, to pursue these issues further and to explore possibilities for cooperative action. Mike Greene, CRN's Director of Government Relations, will be in touch to attempt to set up a meeting as soon as possible.

Respectfully,



Annette Dickinson, Ph.D.  
Vice President, Scientific and Regulatory Affairs

cc: U.S. Sen. Tom Harkin  
U.S. Sen. Orrin Hatch  
U.S. Sen. Edward Kennedy  
U.S. Sen. George Voinovich  
U.S. Rep. Dan Burton  
U.S. Rep. Susan Davis  
U.S. Rep. John D. Dingell  
U.S. Rep. Frank Pallone  
U.S. Rep. Henry Waxman  
The Energy and Commerce Committee  
The Health, Education, Labor and Pensions Committee  
The Government Affairs Committee  
The Government Reform Committee

## CRN RECOMMENDED WARNING LABEL ON EPHEDRA

**WARNING: Not intended for use by anyone under the age of 18. Do not use this product if you are pregnant or nursing. Consult a health care professional before using this product if you have heart disease, thyroid disease, diabetes, high blood pressure, depression or other psychiatric condition, glaucoma, difficulty in urinating, prostate enlargement, or seizure disorder, if you are using a monoamine oxidase inhibitor (MAOI) or any other prescription drug, or you are using an over-the-counter drug containing ephedrine, pseudoephedrine or phenylpropanolamine (ingredients found in certain allergy, asthma, cough/cold and weight control products).**

**Exceeding recommended serving will not improve results and may cause serious adverse health effects.**

**Discontinue use and call a health care professional immediately if you experience rapid heartbeat, dizziness, severe headache, shortness of breath, or other similar symptoms.**