



BACKGROUND

Contact: **Annette Dickinson, Ph.D.**, (202) 776-7951
Acting President
John Hathcock, Ph.D., (202) 776-7955
VP, Nutritional & Regulatory Science

Dietary Supplement Regulation: CRN Responds to *New England Journal of Medicine* Articles Suggesting Legislative/Regulatory Changes

Background

Three articles in the (December 19, 2002) *New England Journal of Medicine* (NEJM) highlight controversies relating to herbal or botanical dietary supplement products. The Council for Responsible Nutrition (CRN), a trade association representing the dietary supplement industry, believes the Dietary Supplement Health and Education Act (DSHEA), the law under which dietary supplements are regulated, provides an adequate framework for dietary supplement regulation but needs further implementation and enforcement.

Dietary supplements have always been regulated in the U.S. as a category of foods. They were considered to be “foods for special dietary use” under the 1938 Food, Drug and Cosmetic Act. In 1994, Congress amended that Act with the passage of DSHEA, defining and in some areas enhancing Food and Drug Administration’s (FDA) authority over dietary supplements. Almost all facets of dietary supplement manufacturing, labeling, and advertising are regulated by FDA or the Federal Trade Commission (FTC).

One of the articles in *NEJM* calls for six changes in the laws or regulations affecting dietary supplement products. CRN notes that some of the suggested changes are already in progress and others can be accomplished by fully implementing the law in its current form. Specifically:

1. Registration of Manufacturers

In some cases, FDA has reported difficulty in contacting companies whose products were the subject of adverse event reports. In most of these instances, the problem is that the reports consumers and physicians submit to FDA often fail to include necessary information such as the product name, the manufacturer shown on the product label, or other factors needed to evaluate the adverse event. CRN’s member companies frequently communicate with FDA and are regularly inspected by both FDA and state regulatory officials—there are no mysteries about the identity or location of these companies. However, for all companies, large and small, registration with FDA will soon be required under the provisions of the new Bioterrorism Act, which requires universal registration of all establishments that manufacture or distribute foods (including dietary supplements) by December 2003.

2. Good Manufacturing Practices

DSHEA provides FDA with authority to develop regulations on specific Good Manufacturing Practices (GMPs) for dietary supplements. CRN has for many years

taken the initiative in supporting strong and effective GMPs for dietary supplements. CRN initially developed GMPs specifically for dietary supplements in the mid-80s, and these were later adopted as the basis for U.S. Pharmacopeia manufacturing guidelines for nutritional supplements. CRN supported the provision of DSHEA relating to GMPs and led the industry in providing a draft document to FDA in 1995. These draft GMPs were published by FDA as an Advance Notice of Proposed Rulemaking (ANPR) in 1997. Now, five years later, we are still awaiting publication of a formal Proposed Rule on dietary supplement GMPs. While progress on this rule has been slow, publication is now expected in the very near future. In the meanwhile, dietary supplements are officially subject to the same GMPs as conventional foods, but most dietary supplement companies and all the trade associations have adopted the more rigorous requirements of the ANPR as their GMP standard. Certification programs established by the U.S. Pharmacopeia and NSF International are also using the ANPR as the basis for their GMP audits. Thus, much progress has been made on the part of the industry toward effectively implementing new GMPs.

3. Premarket Approval

DSHEA requires companies to submit a New Ingredient Notification to FDA before marketing any “new” dietary supplement ingredients (the only class of ingredients that could logically be subject to “premarket” evaluation). It would be helpful for the industry to have more guidance regarding the type of substantiation required in the notification, and FDA has indicated its intention to provide such guidance. Old ingredients are assumed safe (“grandfathered”) unless experience shows otherwise, in the same way that “old” ingredients of foods were grandfathered when the food additive amendments were adopted in 1959. New ingredients of conventional foods can be approved by FDA as food additives or as Generally Recognized as Safe (GRAS), but both of these procedures take many years. FDA permits new ingredients of foods to be self-affirmed as GRAS by manufacturers, and this is the most common avenue today for entry of new food ingredients into the marketplace. Thus, for dietary supplements as well as conventional foods, manufacturers bear the responsibility for the safety of all ingredients, and there are established procedures for introducing new ingredients, not necessarily requiring formal FDA approval.

4. Adverse Event Reporting

Adverse event reporting is an issue that deserves fuller consideration from many perspectives. Mandatory adverse event reporting is currently required only for drugs that are marketed under a New Drug Application, which includes all prescription products but only a small fraction of over-the-counter medications. The vast majority of OTC drugs are not required to report adverse events to FDA. In any discussion of mandatory reporting, attention needs to be paid to distinguishing serious events from minor complaints. There is no mandatory adverse event reporting for conventional foods, infant formulas, medical foods, or dietary supplements. FDA has recently improved its management of adverse event reporting for dietary supplements. Whether additional industry reporting should be required is a topic that has been discussed in a number of Congressional hearings in recent years, and CRN has been a participant in those discussions. We believe it makes sense for the discussion to cover all food and drug categories not currently subject to mandatory reporting, and not be limited to dietary supplements.

5. Product Labeling

DSHEA requires that dietary supplements have full and informative labeling with a list of all ingredients and with a tabular display showing the identity and quantity of all “active” ingredients (dietary supplement ingredients as opposed to excipients such as fillers, colors, and flavors). DSHEA also specifically permits companies to include in their labeling appropriate cautionary or warning statements about possible adverse effects. This provision was included in DSHEA because FDA had sometimes prohibited such warnings, arguing that warnings could be provided only for drug products. Today, cautionary statements, including statements about potential herb/drug interactions, are frequently to be found in the labeling of dietary supplements, and the trade associations have in many cases recommended specific cautionary language.

6. Outside Safety Review

An outside review of dietary supplements already on the market is an idea that has a great deal of appeal to many groups, and numerous expert reviews of botanicals are available. CRN has recently cooperated with the American Botanical Council (ABC) in sponsoring a comprehensive review of the safety and benefits of about 30 top botanical ingredients, and publication by ABC is scheduled for early 2003. The Institute of Medicine has recently released a report outlining a framework for evaluating the safety of dietary supplement ingredients already on the market, and the report is now being evaluated by all interested parties. Also, the NIH Office of Dietary Supplements, established by DSHEA, has an ongoing initiative supporting the preparation of extensive reviews of the safety and benefits of specific dietary supplement ingredients.

Purpose of DSHEA

It should be recalled that the Dietary Supplement Health and Education Act of 1994 and an earlier law affecting dietary supplements, passed in 1976, were both enacted by Congress in response to an enormous outpouring of sentiment from consumers as well as from the affected industry, objecting to FDA initiatives that would have restricted the availability of dietary supplements of vitamins, minerals, botanicals, and other ingredients. Members of Congress on both occasions indicated that they got more constituent mail about dietary supplements than about other burning issues of the day, including the Vietnam War, Watergate, or Desert Storm.

The purpose of DSHEA was twofold: to ensure the continued availability of a variety of safe, beneficial, quality dietary supplements and to provide consumers with access to more information about those supplements. A CRN publication, *Before and After DSHEA*, provides a detailed analysis of the ways in which DSHEA did and did not change the regulatory framework for dietary supplements. Some of the key provisions of DSHEA are as follows:

- DSHEA requires companies to ensure that dietary supplements are “reasonably expected to be safe” under labeled or usual conditions of use. FDA has authority to remove unsafe products from the market, as it has done in several cases (aristolochia, PC-SPES, GHB, and GBL).
- DSHEA requires companies to have substantiation for claims made for dietary supplements. FDA has enforcement authority relating to claims in product labeling, and

has recently made a commitment to be more aggressive in this area. FTC enforces the requirement that product advertising claims be truthful and not misleading, and has pursued numerous cases involving dietary supplements.

- DSHEA requires that dietary supplements actually contain 100% of the amount of each ingredient quantified on the label. Products that fail to meet this requirement are illegally marketed. At the current time, both FDA and state enforcement resources are directed toward products presenting a safety concern, and failure to meet label claim is viewed as a lesser priority. Responsible companies will ensure that their products fulfill consumer expectations, but enforcement will be needed to bring outliers into compliance.

Bottom Line

Dietary supplements provide consumers with an opportunity to be active participants in their own search for health and wellness. CRN and its member companies are committed to supplying the market with safe, beneficial, high quality products and with full and accurate information regarding the usage of those products. DSHEA provides a solid legal and regulatory framework for the continued marketing of dietary supplements, but it needs to be fully implemented. CRN is committed to continuing to work with the regulatory agencies, other segments of the industry, health professionals, and consumer groups in pursuit of full implementation of DSHEA, in order to protect the interests of consumers and of the responsible industry.

NOTE: FDA has just announced (December 18, 2002) that it will step up regulatory enforcement actions against dietary supplements which are in violation of the law, including:

- Seizures of supplements making unsubstantiated structure/function claims.
- Increased inspections of manufacturing plants.
- Pursue criminal cases as appropriate, such as in the promotion unapproved cures for serious diseases.
- Issue warning letters to marketers making disease claims and unsubstantiated structure/function claims.

12/18/02
01/28/03