

USP Quality Review

Botanicals: The Dilemmas Involved in Developing Standards for Natural Products

Part 1 of a 2-part series

In 1820, when the first *United States Pharmacopeia (USP)* was published, nearly two-thirds of the monographs were botanical products. Today, only about two dozen of the over 2,000 entries in the *United States Pharmacopeia 23–National Formulary 18* are botanicals. Historically, plant-derived substances were the cornerstone of medicine. For centuries, most remedies used to treat disease and ailments were taken from plant sources. As technology and scientific methods advanced, techniques for identifying and purifying active components in botanical products emerged. In addition, it became possible to synthesize new agents with enhanced beneficial properties and minimize or eliminate undesirable characteristics. Many modern pharmaceuticals are derived directly or indirectly from plant sources. Similarly, the USP standards have evolved. USP has been establishing the standards for the strength, quality, and purity of drugs and their dosage forms during this period.

The United States has seen a tremendous surge in the use of botanical products as dietary supplements during the

past decade. The trend continues today. Over-the-counter botanical products are a lucrative and rapidly expanding industry. Companies spend millions of advertising dollars marketing these products to the public. Restrictions on dietary supplement labeling and product information, however, have led to implied claims and omitted information about these products. This has generated confusion for consumers and frustration for health care professionals. Moreover, botanical products are produced by many diverse sources, from food manufacturers to major pharmaceutical firms. Although botanical products have been available for many years, many new botanical product lines have recently been introduced. Health care providers and individuals purchasing botanical supplements have expressed concerns regarding the quality, safety, and efficacy of these preparations. In the interest of public safety and continuing commitment to providing authoritative information to health care providers and consumers, the United States Pharmacopeia (USP) resolved to develop standards and information for dietary supplements.

Dietary Supplement Health and Education Act of 1994 (DSHEA)

Renewed consumer interest in natural products and alternative medical therapy has spawned a multibillion-dollar industry of nutrients, health foods, and herbal products. Many consumers did not want the U.S. Food and Drug Administration (FDA) or any government agency interfering with their ability to use a "natural" substance. Americans wanted to ensure their access to these products. New federal legislation governing the regulation of herbs and other botanical substances in products intended for use as dietary supplements was enacted in 1994. The bill, named the Dietary Supplement Health and Education Act of 1994 (DSHEA), amended the Food, Drug, and Cosmetic Act.

This legislation extended the definition of dietary supplements, revised their classification, and amended the requirements for labeling and accompanying literature. Previously, dietary supplements were considered to be only essential nutrients; now the definition has been expanded to include botanical products (see Figure 1).

Figure 1

DSHEA Definition of a Dietary Supplement

A dietary supplement is defined as a "product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

- a vitamin
- a mineral
- an herb or other botanical
- an amino acid
- a dietary substance for use by man to supplement the diet by increasing the total dietary intake
- a concentrate, metabolite, constituent, extract, or combination of any of the former ingredients.

Dietary supplements are available for ingestion as tablets, capsules, powders, softgels, gelcaps, or liquids. They are not represented as conventional foods or as solo items of a meal or the diet.

Highlights of the major provisions of this legislation include:

Dietary Supplements Are Deemed to Be Foods:

The DSHEA considerably altered the way FDA regulates dietary supplements. Botanical products historically used for medicinal purposes are currently subject to the same regulations governing food products in the United States. The FDA's Center for Food Safety and Applied Nutrition (CFSAN) has authority over botanical products used as dietary supplements. The center does not approve these products prior to marketing. In addition, manufacturers of dietary supplements are not bound by the stricter regulations that govern prescription and nonprescription medications overseen by the FDA's Center for Drug Evaluation and Research (CDER). Although the legislation authorizes the FDA to establish "good manufacturing practice" (GMP) regulations, it indicates that the regulations be modeled after the GMP guidelines in effect for the food industry, which principally deal with issues of sanitation.

Safety Requirements:

Dietary supplements are not subjected to a rigorous evaluation of their safety in use before they are brought to market. According to the legislation, botanical products are deemed "adulterated" if they "present a significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling, or if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use." The "burden of proof" that a botanical is unsafe is placed upon the FDA. In contrast, manufacturers of new drug products are responsible for proving the safety of their products prior to marketing.

Product Statements and Labeling Requirements:

Prior to the DSHEA, dietary supplements possessing labeling information that professed health claims would be considered "misbranded" by the FDA. The new legislation allows manufacturers of dietary supplements to make statements of nutritional support, particularly claims describing the supplements intended influence on body structure or function (see Figure 2).

These claims, however, may only be made if the manufacturer is able to substantiate that the claim is "truthful and not misleading." The FDA does not evaluate these statements before the product is marketed. Manufacturers are required, however, to notify the FDA "no later than 30 days

after the first marketing of the dietary supplement." Products bearing nutritional support statements must also prominently display 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."

All labels should contain a phrase identifying the product as a dietary supplement, list the name and quantity of each ingredient, and in the case of botanical products, identify the part of the plant from which it is derived.

Compendial Specifications:

The legislation maintains that dietary supplements claiming to meet the specifications of an "official compendium" will be deemed "misbranded" if they fail to meet the specifications. Therefore, products bearing the "USP" (*United States Pharmacopeia*) or "NF" (*National Formulary*) symbols are required to comply with the compendial standards. In contrast, official drug products must adhere to "USP" or "NF" standards whether or not the labeling contains the designation "USP" or "NF."

The next issue of *USP Quarterly Review* will cover the challenges in developing standards for natural products.

Figure 2

Types of Statements of Nutritional Support Appearing on Dietary Supplements

1. Claims of a benefit related to a classical nutrient deficiency disease and disclosure of the prevalence of the disease in the United States (e.g., iron prevents iron deficiency anemia, a blood disorder sometimes found in women).
2. Descriptions of the role of a nutrient or dietary ingredient intended to affect the structure or function in humans (e.g., calcium helps build strong bones).
3. Characterizations of the documented mechanism by which the nutrient or dietary ingredient acts to maintain such structure or function (e.g., garlic helps maintain healthy cholesterol levels).
4. Descriptions of general well-being from consumption of a nutrient or dietary supplement (e.g., St. John's Wort helps maintain a healthy emotional balance).

To report product quality problems or to receive further information, call the USP Practitioners' Reporting NetworkSM at 800-487-7776. For your convenience the DPPR reporting form is also available on-line at www.usp.org

