

# Regulation of Dietary Supplements and Nutraceutical Products in the United States: An Argument for Greater Oversight and Uniform Standards

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On behalf of the ACCP Public Policy Committee

The American College of Clinical Pharmacology (ACCP) recognizes the importance and contribution of dietary supplements and nutraceutical products to individual and public health. We seek a call to action on improving the regulatory framework of dietary supplements and nutraceutical products to ensure health care professionals, consumers, and patients have access to safe and adequately labeled products. The ACCP believes that strengthening the current regulations by implementing more stringent Good Manufacturing Practices (GMP), labeling, promotional standards and activities, and establishing scientific monographs for existing products will improve public health and reduce the burden of illness due to drug interactions, adulterants, and contaminations.

Dietary supplements encompass products that are taken by mouth to supplement the diet and, by law, cannot be used to diagnose, treat, cure, or prevent any disease. However, these products are commonly used to self-treat various ailments. These products include vitamins and herbal products of varying composition. About 50% of US adults take at least 1 dietary supplement and between 20% and 30% are taking at least 1 prescription drug concomitantly with a dietary supplement, increasing their risk for a supplement-drug interaction.<sup>1</sup> The current regulatory framework is based on the 1994 Dietary Supplement Health and Education Act (DSHEA), which provided the US Food and Drug Administration (FDA) and the Federal Trade Commission with the authority to oversee certain aspects of dietary supplement regulation such as limited GMP and labeling standards. However, the burden of proof for demonstrating safety concerns is with the FDA, and efficacy need not be shown before marketing of a dietary supplement. Furthermore, implemented GMP guidelines require only internal consistency in

product quality and limited testing for contaminants, which results in the sale of many dietary supplements containing heavy metals, adulterants including deliberate addition of prescription medications and synthetic illicit substances, microbial contamination, and different herbal/plant species or different doses or strengths than labeled.<sup>2–5</sup> Key differences between FDA-approved drugs that have to adhere to part 211 of the GMP guidance and dietary supplements that follow part 111 of the GMP guidance are in raw material and finished product testing, which are mostly optional for dietary supplements, no stability or shelf-life testing requirement, and no documentation of change control for dietary supplements.

Critiques of the DSHEA by professional organizations in the early and mid-2000s led Congress to enact the Food Safety Modernization Act in 2010 that provided the FDA with some additional authority to enact import bans on certain dietary supplements and nutraceutical products not marketed before enactment of the DSHEA as well as to require premarket safety data on new dietary ingredients.<sup>6</sup> While this distinction has increased the threshold for approval of new dietary supplements, it does not address the current quality issues of dietary supplements that were grandfathered in under the DSHEA and available on the market before 1994. Furthermore, the Food Safety Modernization Act fails to require any proactive regulatory review or approval before bringing a supplement to market. It is only after the fact where an investigation has

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been triggered through various mechanisms such as product complaints or safety reports that leads to legal enforcement. Indeed, reports indicate that the problem is ubiquitous in the marketplace. In a 2015 investigation by the New York State Attorney General's office of popular supplement products at 4 large national chain retailers (GNC, Target, Walgreens, and Walmart), it was found that 79% of herbal products tested did not contain DNA from the plant species listed on the label.<sup>7</sup> A more comprehensive analysis of herbal product authenticity, as detected with DNA-based methods, of 5957 commercial herbal products sold in 37 countries found that ≈27% of the herbal products commercialized in the global marketplace, including 33% of herbal products in North America, were adulterated against their labeled, claimed ingredient species.<sup>7,8</sup>

The limited oversight of dietary supplements and nutraceutical products has provided a landscape for marketing that often leads to misinformation and confusion for health care professionals, consumers, and patients when choosing such products. In addition to the risks of mislabeled, adulterated, and contaminated products, the labels do not contain adequate information on safe use especially in regard to drug interactions, dosing, and potential adverse effects.<sup>9,10</sup> An unrelated but equally important dimension concerns the lack of knowledge of dietary supplements<sup>11</sup> and other complementary and integrative medicines by health care professionals that often lead consumers and patients to avoid disclosing their use or consulting with them.<sup>12,13</sup> Health care professionals are reluctant to recommend or even engage with patients to discuss the use of dietary supplements or other complementary and integrative medicines because of the current lack of regulation and clinical data and mistrust of unproven, unreliable, and variable quality of dietary supplements flooding the market.<sup>14,15</sup>

The current lack of regulatory oversight and transparency has created insecurity for health care providers, patients, and manufacturers alike. Although the United States Pharmacopeia (USP), a nongovernmental private but independent entity, has developed a few monographs for pure dietary supplement ingredients such as vitamin E (alpha tocopherol), standardized herbal extracts such as St. John's wort (*Hypericum perforatum*), and live probiotic bacterial strains such as *Lactobacillus rhamnosus*. Manufacturers can elect and pay to be subjected to USP quality control, which then permits display of the USP-verified mark on that particular product. Though such products with the USP verification have acceptable quality, USP is not a government agency, and such testing is not enforced. Furthermore, it does not solve the issue of supplement-drug interactions and needed research on safety and

effectiveness on dietary supplements and nutraceutical products.

The ACCP is calling on stakeholders to strengthen governmental oversight and provide regulatory agencies (ie, FDA and Federal Trade Commission) with the necessary mandate through acts of Congress to implement standards that allow for accuracy in labeling and transparency in scientific information on safety and composition of dietary supplement and nutraceutical products. Consistency in product composition should be assured through standardization of herbal and other complex extracts by eliminating "proprietary" blends of undisclosed ingredients. Limits for contamination with pesticides, heavy metals, illicit or prescription substances, or other unidentified compounds in supplements should be established to further reduce the risk of adverse outcomes. Funding sources to expand dietary supplement monographs (as part of ongoing USP initiatives) and provide preclinical and clinical safety and efficacy data on dietary supplements and nutraceutical products should be made available in the interest of public health and health care provider trust.

## Conflicts of Interest

M.R. and O.G. are employees of the University of Florida. P.K. is an employee of Gilead Science, Inc.

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## Disclaimer

The opinions expressed in this article are those of the authors on behalf of the American College of Clinical Pharmacology and should not be interpreted as the position of the entities or institutions at which the authors are employed.

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