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# HERBAL REMEDIES AND DIETARY SUPPLEMENTS: THE BOUNDARIES OF DRUG CLAIMS AND FREEDOM OF CHOICE

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## I. INTRODUCTION

On the eve of the landmark 1994 election, the Democratically-controlled Congress unanimously passed, and President Clinton signed, the Dietary Supplement Health and Education Act (DSHEA).[1] That law exempted claims about the effects of dietary supplements on the human body[2] from the drug provisions of the Federal Food Drug and Cosmetic Act (FFDCA).[3] DSHEA also exempted supplements from other

1. Pub. L. No. 103-417, 108 Stat. 4325 (1994) (codified as amended in various sections of 21 U.S.C.). DSHEA became law on Oct. 25, 1994. *Id.* In the November election, the Republican party became a majority in both houses of Congress. Adam Clymer, *G.O.P Celebrates Its Sweep to Power, Clinton Vows to Find Common Ground*, N.Y. TIMES, Nov. 10, 1994, at A1.

2. 21 U.S.C. §§ 321(g)(1) & 343(r)(6)(A) (1994).

3. 21 U.S.C. §§ 301-397.

provisions of the FFDCA and established new standards for claims and safety determinations for supplements.[4]

At the same time, DSHEA defined dietary supplements broadly to include herbs and other dietary substances used to supplement the diet.[5] Dietary supplements have long included vitamins and minerals. Over time, products have been sold as supplements that did not have a recognized nutritional value, and even some without a history of use in foods, and with a use in traditional medicine.[6] Under DSHEA, dietary ingredients need not be nutrients, but the law has not provided guidance on the broader new meaning of the term "dietary."[7] The enactment of DSHEA became a harbinger of a new era of re-examination of the appropriate limits of regulatory power. Indeed, the term "being DSHEAed" has become a byword for deregulation in some quarters.

This Article examines the changes made by DSHEA. While, under DSHEA, the supplement manufacturers cannot make disease treatment and prevention claims on the supplement labels, they now can make "statements of nutritional support" claiming effects on the "structure or function" of the body.[8] Before DSHEA, claims of this type for non-nutritional supplements would have been regarded as drug claims subject to the pre-market approval and controlled testing ordinarily required for drugs.[9] This change creates ambiguity concerning the boundary between drug claims and food claims. DSHEA also removes "publications" that provide scientific information in connection with supplement sales from the scope of the FDA's ability to regulate labeling claims (the "publication exemption"), opening up the possibility for disease treatment and

4. 21 U.S.C. § 321(s) (exemption from food additive definition); 21 U.S.C. § 343-2 (publication exemption); 21 U.S.C. § 343(r)(6) (statements of nutritional support); 21 U.S.C. §§ 342(f), 350(b) (1994) (new safety provisions for supplements).

5. 21 U.S.C. § 321(ff) (1994).

6. *See FDA Advance Notice of Proposed Rulemaking*, 21 C.F.R. ch. 1, *Regulation of Dietary Supplements*, 58 Fed. Reg. 33,690, 33,697 (1993), *reprinted in* BASS & YOUNG, *infra* note 56, at 307-19 (FDA notice reviewing history of regulation of dietary supplements) [hereinafter *FDA Advance Notice*].

The term "botanical" encompasses all plants, including herbs, which are "seed producing" plants without "persistent woody tissue." WEBSTER'S THIRD NEW INTERNATIONAL DICTIONARY 258 (1963) (botanical); *id.* at 1058 (herb). This Article generally refers to "herbal remedies" because of the greater familiarity of that term among consumers, but uses the term "botanical products" when referring to the scientific recommendations of the Commission on Dietary Supplement Labels. *See infra* text accompanying note 15.

7. 21 U.S.C. § 343(r)(6) (1994); *infra* pts. III.B. & C.

8. 21 U.S.C. § 343(r)(6)(A) (1994).

9. *See* Nutrilab, Inc. v. Schweiker, 713 F.2d 335 (7th Cir. 1983); discussion *infra* pt. II.C.; 21 U.S.C. § 355 (1994); *infra* pts. IV.A. & B. for a discussion of the new drug requirements and the ways of satisfying the legal requirements governing drugs.

prevention claims to be made for dietary supplements.[10] As a result of DSHEA, a vast range of new claims are being made regarding the effects of supplements, including assertions that they help one think better, improve the immune system, lower cholesterol, and are herbal versions of prescription drugs.[11]

DSHEA also revoked the authority of the Food and Drug Administration (FDA) to require pre-market approval of the safety of dietary supplements, an authority that also had been narrowed by court decisions.[12] The enactment of the safety provision of DSHEA has been called Commissioner Kessler's "greatest failure" in his years as the head of the FDA.[13] Kessler has commented that there are "certain problems you are not going to solve" and dietary supplements are "one of them."[14]

This Article considers ways to implement DSHEA and methods that may be used to provide additional protection to consumers even with the reduced powers given to the FDA. It examines ways to distinguish nutritional support statements from inappropriate claims by considering factors to identify disease treatment and prevention claims, and the "dietary" role of supplements. The Article discusses the type of testing that manufacturers need to do to substantiate the claims made for supplements. Manufacturers of supplements also should have an enforceable obligation to substantiate the safety of all supplements, and the FDA should be able to determine effectively whether manufacturers have met their legal obligations of substantiating the safety of products and any claims they make. In addition, this Article examines whether the publication exemption should apply only to articles containing scientific information that are written independently from manufacturers. If the law can be interpreted as this Article suggests, the additional safeguards will help provide minimal consumer protections while further experience tests how well the DSHEA regulatory model works.

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10. 21 U.S.C. § 343-2 (1994). The Federal Trade Commission (FTC) may regulate misleading claims in publications that contain advertising, but its authority is different from the FDA's and does not encompass pre-market approval of drug claims. *See* 15 U.S.C. §§ 45, 52 & 55 (1988).

11. *See* discussion *infra* pts. III.C.1. & C.2.b.

12. *See* 21 U.S.C. § 321(s)(6) (1994). For judicial decisions, see United States v. Oakmont Inv. Co., 937 F.2d 33 (1st Cir. 1993); United States v. Vipone Ltd. Black Currant Oil, 984 F.2d 814 (7th Cir. 1993); *infra* pt. III.E.2.

13. *See* Marian Burros, *F.D.A. Commissioner Is Resigning After 6 Stormy Years in Office*, N.Y. TIMES, Nov. 26, 1996, at A1 ("Others see his inability to keep dangerous dietary supplements off the market as his greatest failure. Under significant pressure from the dietary supplement industry Congress passed legislation . . . to exempt from strict oversight supplements like ephedra, which has caused several deaths.").

14. *Id.* at A18.

When Congress enacted DSHEA, it created an independent Commission on Dietary Supplements Labels (the Commission), to provide recommendations on the use of health and other claims on dietary supplements.[15] I served as one of seven members appointed by the President to the Commission, which issued its final report in November 1997.[16] While this Article is an outgrowth of my work on the Commission, it reflects my views of the larger issues raised by that project. The Article provides an analysis from a legal and academic perspective of only some of the issues covered by the report. Moreover, on a number of points, I stated views in the report that differed from other Commissioners or went beyond the recommendations of the Commission as a whole. This Article reflects my personal views and is not a restatement or summary of the work of the Commission.

Another major focus of this Article is the Commission's recommendation that a study be performed of an alternative system based on international models for regulating therapeutic claims for herbal or botanical supplements. In its report, most of the Commissioners concluded that consumers would be better served by clear information about the traditional therapeutic uses of botanicals when they have scientific support, rather than by the use of DSHEA to suggest such uses without overtly stating them, a process which may "create a climate of deception that serves neither the industry nor consumers."[17] The Commission recommended a study of international models and "some alternative system, for regulating the use of botanical remedies that do not meet the requirements in this country for over-the-counter (OTC) drugs."[18] The Commission did not expressly recommend any lower standard of approval for botanical remedies, but such a possibility is inherent in a study of an alternative system for products that do not meet the existing legal standards for drugs.

The recommendation for a study of an alternative system raises difficult and important issues about whether there should ever be a different standard for approval of disease treatment and prevention

15. 108 Stat. 4332 (codified at 21 U.S.C. § 343 note).

16. COMM'N ON DIETARY SUPPLEMENT LABELS, COMM'N ON DIETARY SUPPLEMENT LABELS REACT TO THE PRESIDENT, CONGRESS, AND THE SECRETARY OF THE DEP'T OF HEALTH AND HUMAN SERVICES (Nov. 1997) [hereinafter COMMISSION REPORT]. The Commission report, issued November 24, 1997, is available from the Government Printing Office 017-001-00531-2 and on the Internet at http://web.health.gov/dietsupp.

This Article presents the perspective I gained from my work on the Commission and focuses on the developments at the time the work of the Commission was completed.

17. *Id.* at 56-57.

18. *See id.* at xi & 57. The issues concerning the scope of any alternative category are discussed *infra* pt. V.

claims for some drugs and not others, as well as the safeguards that would be needed. An alternative system can have different rationales. Some may believe that efficacy can be adequately determined, based on traditional use without controlled testing. The rationale that warrants study, in my view, would not regard traditional use as an adequate basis for determining efficacy, but would consider whether consumers should have the freedom to use safe drugs not adequately proven to be effective when these consumers are clearly and adequately informed about the lack of testing. More investigation is needed concerning whether there are adequate ways to protect consumers under such an approach.

Whether an alternative system for therapeutic claims on botanical remedies would be better than the use of DSHEA to suggest such claims presents a conundrum. Comparison is difficult because alternative systems have yet to be studied and debated. Moreover, what is permissible under DSHEA is itself ambiguous. Importantly, additional guidance concerning the scope of permissible claims under DSHEA may help eliminate some of the most questionable uses of nutritional support statements to imply effectiveness for disease prevention and treatment. Thus, regulatory action to address inappropriate claims under DSHEA may indirectly reduce the need for an alternative system as a way of protecting consumers from ambiguous claims.

If an alternative system is to be considered for botanical products, thought also must be given to whether the alternative system should encompass safe but unproven remedies for those suffering from life-threatening and seriously debilitating illnesses such as cancer, AIDS, blindness, and Alzheimer's disease. To prevent harm, use of these products, even under a freedom-of-choice rationale, should still be limited to use after consultation with a physician. The physician also should be provided by the manufacturer with adequate information concerning the deficiencies in the supporting evidence for the product that the physician can use in advising the patient. Potent products and supplements that pose risks of harm should continue to be governed by the approval procedures governing new drugs.[19]

Finally, the existing legal system already indirectly provides a way for consumers to exercise the freedom to use supplements for disease prevention and treatment purposes by the very availability of products sold simply as dietary supplements. Americans have an increasing

19. *See, e.g.*, 21 U.S.C. § 355 (governing the introduction of new drugs into interstate commerce); Pub. L. No. 105-115, §§ 112 & 402, 111 Stat. 2296, 2309-10, 2365-67 (enacting §§ 506 and 551, to be codified as amended at 21 U.S.C. §§ 351 *et seq.*) (expediting the study and approval of fast track drugs and regarding the dissemination of information on new drug uses).

interest in herbal remedies as well as in other alternatives to standard health care.[20] When products are sold as "dietary supplements," the consumer is, and has long been able to use the supplements for therapeutic uses not stated on the label.[21] DSHEA safeguards the availability of botanical and other dietary supplements even though consumers may be using the products, on their own initiative, for drug purposes. This means of giving consumers freedom-of-choice is imperfect, but developing an alternative system of doing so also presents difficulties. The political compromise represented by DSHEA is likely to continue to have an important role in indirectly giving Americans the choice to use supplements for disease purposes on an "off-label" basis.[22]

Part II of this Article reviews the FDA's efforts to regulate dietary supplements and its jurisdictional authority to regulate products as drugs. That history provides perspective on the purpose, scope, and impact of DSHEA. Part II also shows the difficulties the FDA has long had in regulating dietary supplements as drugs based on consumer use in the absence of claims attributable to the manufacturer.

Part III examines the new provisions of DSHEA that bear on the ability of supplement manufacturers to make claims about the effects of supplements on the body and analyzes tests for distinguishing dietary supplement claims from inappropriate claims for disease prevention and treatment or non-dietary effects claims. Part III also considers the scope

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20. *See, e.g.*, ISADORE ROSENFELD, DR. ROSENFELD'S GUIDE TO ALTERNATIVE MEDICINE 1 (1996) (noting that millions of Americans, especially the better educated, are spending "billions" every year on "a wide variety of 'alternative, complementary,' or 'holistic' therapies such as herbs, acupuncture, and meditation"); *see generally* Michael H. Cohen, *A Fixed Star in Health Care Reform: The Emerging Paradigm of Holistic Healing*, 27 ARIZ. ST. L.J. 79 (1995) (examining the extent to which the legal system accommodates holistic healing methods); David M. Eisenberg et al., *Unconventional Medicine in the United States: Prevalence, Costs, and Patterns of Use*, 328 NEW ENG. J. MED. 246, 28 (Jan. 28, 1993) (reporting results of a survey in which one-third of the American respondents reported using at least one unconventional therapy in the previous year, and one-third of those saw unconventional therapy providers).

21. A notable example of consumer use of a dietary supplement for an off-label drug purpose was reported by the *New York Times* personal health editor who used a supplement as a remedy for an arthritic knee. *See* Jane E. Brody, *Personal Health*, N.Y. TIMES, Jan. 15, 1997, at C10 ("I am only an anecdote of one, not a study that proves anything. Without a careful scientific study, any personal account of benefit leaves open to question what actually caused the improvement.").

*See generally* Scott Martin, Note, *Unlabelled "Drugs" as U.S. Health Policy: The Case for Allowing Health Claims on Medicinal Herb Labels; Canada Provides a Model for Reform*, 9 ARIZ. J. INT'L & COMP. L. 545 (1992) (examining "the regulation of medicinal herbs in the United States and Canada," and suggesting "that the FDA has the authority to regulate medicinal herbs by a less restrictive 'effectiveness' standard than that used for conventional drugs").

22. *See infra* note 60 and accompanying text.

of the publication exemption, the new provisions governing the safety of supplements, and the need to ensure that the FDA has sufficient authority to deal with safety and enforcement issues.

Some botanical products already may have the type of testing and support necessary to be appropriately sold as OTC drugs under the present law. Part IV of this Article considers the FDA's OTC review program and the recommendations made by the Commission to encourage the FDA to develop a process for evaluating botanical remedies when the manufacturer has the studies and other support needed for approval under the existing law.

Part V of this Article discusses the different rationales for an alternative system of regulation for botanical remedies that would use a less stringent standard. The advantages and drawbacks of these rationales for an alternative system are examined in relationship to DSHEA as a means of providing freedom of choice to consumers.

This Article specifically focuses on issues involving supplements that consumers may use for therapeutic purposes. There are, however, many dietary supplements that clearly are used by consumers only for nutritional purposes. (One-a-day vitamin pills are the most obvious example.) Discussion of such supplements is beyond the scope of this Article.

## II. THE FDA'S EFFORTS TO REGULATE DIETARY SUPPLEMENTS AND THE JUDICIAL AND CONGRESSIONAL RESPONSE: THE ROAD TO DSHEA

The history of the FDA's regulation of dietary supplements is important in understanding the factors that led to the enactment of DSHEA, and the role that supplements have increasingly played in providing consumers with individual choices. A "bitter battle" has occurred between the FDA and the dietary supplement industry about when supplements can be considered to be drugs.[23] In regulating supplements, the FDA has tested the limits of its ability to regulate a product as a drug based on various ways of determining the manufacturer's intent. The agency has had some important victories over legal principles, but legislative changes and court decisions have substantially limited the FDA's authority to regulate supplements as drugs based merely on consumer use without other evidence to show the seller's intent to market the product as a drug.

23. The phrase is Judge Friendly's, who presided over some of the more contentious chapters. National Nutritional Foods Ass'n v. Kennedy, 572 F.2d 377, 379 (2d Cir. 1978); *see also infra* note 55.

### A. *Early History of Court Enforcement and Broad Interpretation of Labeling*

Any ingested product, including a supplement, that is intended by its manufacturer to prevent or treat a disease is a "drug" under the law.[24] Products (other than foods) that are intended to affect the structure or function of the body are also considered drugs.[25] Misleading drug claims originally were prohibited by the FFDCA as enacted in 1938.[26] The drug efficacy amendment, enacted in 1962 in the wake of the thalidomide tragedy, went further in requiring prior FDA approval of drug effectiveness claims, based on adequate and well-controlled studies, unless the product was generally recognized by experts as effective based on similar studies.[27]

In the early years, vitamins, minerals, and herbs often were the subject of FDA enforcement actions, which sometimes were based on the FDA's authority to preclude misleading claims on foods.[28] The FDA also would assert that the claims made for the product, in one way or another, suggested a therapeutic purpose that did not meet the applicable standards for drugs.[29]

The FDA had success in establishing a wide scope for its authority to reach the indirect means used by manufacturers to make these drug effectiveness claims. In a landmark case from the 1940s, involving vitamins, the United States Supreme Court held that the "labeling" covered by the Act included pamphlets mailed separately by the manufacturer to retailers even when the material was not physically attached to the product itself.[30] The Court found that the pamphlets performed the function of labeling by explaining the product's use, and gave labeling a broad reading to ensure that the law not "be circumvent-

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24. *See* 21 U.S.C. § 321(g)(1)(B) (defining "drug" in part as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease").

25. 21 U.S.C. § 321(g)(1)(C); *see* discussion *infra* pt. III.C. (regarding the non-applicability of this provision to statements of nutritional support for dietary supplements under DSHEA).

26. *See* 21 U.S.C. § 352(a) (1994) (including legislative history).

27. *See* 21 U.S.C. § 355 (requiring filing and approval of an application prior to delivering into interstate commerce any "new drug"); Weinberger v. Hynson, Westcott & Dunning, Inc., 412 U.S. 609, 612-15 (1973) (discussing the historical development of the amendments concerning drug efficacy); see *infra* pt. IV for further discussion of the efficacy provisions.

28. *See* 21 U.S.C. § 343(a)(1) (pertaining to false or misleading labels on food).

29. *See* V.E. Irons, Inc. v. United States, 244 F.2d 34 (1st Cir. 1957); PETER B. HUTT & RICHARD A. MERRILL, FOOD & DRUG LAW: CASES AND MATERIALS 207 n.2 (2d ed. 1991) ("The *Irons* case is illustrative of literally hundreds of court actions . . . against false or misleading nutritional claims . . . under the food and drug sections of the Act.").

30. *See* Kordel v. United States, 335 U.S. 345, 349 (1948) (construing §§ 301(a), 502(f) & 201(m), in relationship to false labeling).

ed."[31] Courts have recognized, however, that labeling does not include books and written material by an independent author that may state potential drug uses for a product, absent some showing of an integrated plan to use the material to make claims for a product at the point of sale, even though the writings are sold in the same store as the product.[32]

The FDA and the Federal Trade Commission (FTC) brought hundreds of court actions against misleading claims and advertisements for nutrition products and "undoubtedly expended more enforcement resources in the area of nutrition than in any other single field" through the 1960s.[33] This case-by-case enforcement approach, however, had limited effectiveness, and ultimately the FDA looked to the use of rulemaking as a means to regulate claims on supplements.

### B. *FDA Regulations and Response: Consumer Use and Drug Intent*

In rules issued in the 1940s, the FDA recognized the food value of certain dietary supplements, but did not seek to preclude claims for other supplements, and instead required a label disclaimer stating that the need for the substance "in human nutrition has not been established."[34] The FDA later became dissatisfied with the disclosure, because consumers might read it as suggesting that evidence of nutritional value was imminent.[35]

In 1962, the FDA began a regulatory effort to withdraw the "crepe labeling," and limit dietary supplements containing vitamins and minerals to uses for which there was a recognized nutritional need.[36] The FDA sought to refute the "myths of nutrition": that the modern processing of foods "strips them" of virtually all nutritional value, that it is "essentially impossible to obtain from our daily diets the nutrients we require," and that nearly everyone may suffer "from a subclinical nutritional deficiency."[37]

The difficulty was that many consumers and even some professionals believed in the "myths," and also believed that "optimal" nutrition

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31. *See id.* at 350.

32. *See* United States v. Sterling Vinegar & Honey, 338 F.2d 157, 158 (2d Cir. 1964).

33. HUTT & MERRILL, *supra* note 29, at 207 n.2.

34. *See, e.g.*, 6 Fed. Reg. 5921, 5925 (Nov. 22, 1941); 6 Fed. Reg. 3304, 3310 (July 8, 1941); 5 Fed. Reg. 3565 (Sept. 5, 1940).

35. *See* William W. Goodrich, *The Coming Struggle over Vitamin-Mineral Pills*, 20 BUS. LAW 145 (1964). Mr. Goodrich was, at the time he wrote his article, the Chief Counsel for the FDA.

36. 27 Fed. Reg. 5815 (June 20, 1962).

37. *See* Goodrich, *supra* note 35, at 147.

required doses in excess of that needed to avoid clinical deficiencies.[38] They resisted the FDA's regulatory effort with fervor. The final regulations, issued in 1973 after a long administrative hearing, prohibited irrational combinations of vitamins and minerals when sold as foods, and set the maximum and minimum potency of the recognized food nutrients.[39] In addition, high doses were to be considered drugs under the drug definition, even in the absence of any explicit drug claim by the manufacturer, because of the lack of any nutritional need for a higher dose.[40]

On judicial review, the agency won a partial, temporary victory. Judge Friendly found that the agency had the authority to protect consumers from confusion about the food value of supplements by limiting combinations and doses of vitamins and minerals.[41] Consumers who wanted nutrients above the levels set by the regulations were not prohibited from ingesting more; they could simply "take as many more tablets" as they liked.[42] The court remanded the regulations, however, for further consideration of exceptions and changes in some of the dosage levels.[43]

With respect to the classification of high-dosage nutrients as drugs, the court found that a product is a drug only if the manufacturer intends its use for drug purposes.[44] A manufacturer's actual intent could be determined on the basis of "objective evidence," and a factfinder was not bound by a manufacturer's subjective claims.[45] More was needed to show an actual therapeutic intent based on objective evidence, however, than a mere lack of nutritional usefulness, the basis relied on by the FDA.[46] Indeed, the court recognized that some consumers have particularly high nutritional needs.[47]

Following the decision and the FDA's victories on points of legal theory, supplement manufacturers and users were "outraged" and

38. *See* National Nutritional Foods Ass'n v. FDA, 504 F.2d 761, 789, 791 (2d Cir. 1974).

39. *See* 38 Fed. Reg. 20,708, 20,730 (1973).

40. *See id.*

41. *See National Nutritional Foods*, 504 F.2d at 789-92.

42. *See id.* at 792.

43. *See id.* at 808.

44. *See id.* at 789.

45. *See id.* The determination of the manufacturer's intent also can be found in labeling, promotional material, advertising, and other material for which the promoter is responsible. *See* United States v. Sudden Change, 409 F.2d 734, 739 (2d Cir. 1969).

46. *See National Nutritional Foods*, 504 F.2d at 789.

47. *Id.* The petitioners also maintained that there was a "fairly widespread if minority belief that the 'optimal' level of nutrition" was higher than the levels set by the FDA to avoid clinical deficiencies. *Id.* at 791.

lobbyed Congress for a change.[48] Congress responded by enacting the "Proxmire amendment," which revoked the FDA's authority to regulate vitamins and minerals as foods based on irrational combinations or potency limits.[49] In addition, the FDA could not classify a vitamin or mineral as a drug "solely because it exceeds the level of potency which [the FDA] determines is nutritionally rational or useful."[50]

The FDA responded by seeking to regulate some supplements on the basis of what remained of its authority under the judicial precedent, notwithstanding the legislative amendment. The FDA sought to show that high doses of Vitamins A and D were drugs based on objective evidence of manufacturer's intent, not because of their lack of nutritional usefulness, but because the promotion of those vitamins by others had led to such widespread therapeutic use by consumers that such use outweighed their use as dietary supplements.[51] On review, the court, with a different panel, found the evidence of intent insufficient because the FDA had not shown that consumer use for therapeutic purposes corresponded to the particular dosage level which the FDA had used to classify the vitamins as drugs—a level that the FDA had based on safety considerations.[52] Some consumers used lower levels for drug purposes; some used higher levels based on their views of the nutritional value at that level.[53] The court demanded a high standard of proof to show objective intent: the use must be widespread and involve use of the particular dose level by the consumer for a knowing therapeutic use, and not simply consumer use for a nutritional purpose that experts might regard as mistaken and confused.[54] The interpretation was in line with the broader impact of the Proxmire amendment in making it harder for FDA to classify supplements as drugs.[55]

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48. Mark A. Kassel, *From a History of Near Misses: The Future of Dietary Supplement Regulation*, 49 FOOD & DRUG L.J. 237, 257 (1994).

49. *See* 21 U.S.C. § 350 (1994) (originally enacted 1976).

50. *Id.* § 350(a)(1)(B).

51. National Nutritional Foods Ass'n v. Mathews, 557 F.2d 325, 329 (2d Cir. 1977).

52. *See id.* at 337-38.

53. *See id.*

54. *See id.*

55. A larger significance of the Proxmire amendment was suggested by Judge Friendly in a related case when the FDA tried to re-issue certain aspects of its food supplement regulations that had been remanded in *National Nutritional Foods*, 504 F.2d at 761. The court found that Congress was not concerned about the risk of consumer confusion over food issues that had been the basis for the original regulations, or, at least, that Congress considered the costs "too high" in relation to the benefits. While the FDA still had the legal authority to issue the particular regulations, the court required the agency to take further public comment on whether there was a sufficient consumer need for them. *See Kennedy*, 572 F.2d at 385. In the end, the FDA withdrew the entire regulatory scheme.

### C. *Scaled-Back Enforcement and Expansion of Supplement Uses*

After the Proxmire amendment, the FDA scaled back its enforcement efforts with respect to supplements. The amendment and the court decisions "dissuaded the agency from routinely regulating these products."[56] Under its food authority, the FDA would enforce the requirements for pre-market approval of the safety of a food additive when a specific safety concern arose, rather than because of the lack of information about the supplement. The agency brought enforcement action under its drug authority when the labeling "contained" unauthorized drug claims.[57]

This policy of restraint made it easier for additional types of products to be sold as supplements, resulting in a significant expansion in the number of supplements on the market by the 1990s.[58] Shark cartilage and herbs used in traditional medicine joined the vitamins and minerals in the health food stores. The FDA would not take enforcement action against these new types of supplements unless there were identified safety concerns, or unless the manufacturer made express drug claims in labeling or promoted the products as drugs through advertisements or other means.[59]

The availability of these products permitted "off-label" uses by consumers.[60] Popular literature, books, or other sources might identify the supplements as having a disease treatment value not suggested in the labeling. Some consumers might also know from their own experience of traditional therapeutic uses. Thus, consumers could use these products for medicinal purposes, but the manufacturers would face enforcement

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56. General Accounting Office Report to Senator Kennedy, at 4 (B252966, July 2, 1993), *reprinted in* I. SCOTT BASS & ANTHONY L. YOUNG, DIETARY SUPPLEMENT HEALTH AND EDUCATION ACT: A LEGISLATIVE HISTORY AND ANALYSIS 297, 300 (1996).

57. *Id.*

58. FDA Advance Notice, 58 Fed. Reg. at 33,698-99 (1993). Congress required the FDA to revoke this notice but it remains of historical value. *See infra* text at pt. III.B.1.

59. *See* General Accounting Office Report, *supra* note 56.

60. The term "off-label use" is a common informal reference to the use of an approved drug by a physician for a use not approved by the FDA, which raises issues analogous to consumer use of dietary supplements for unapproved purposes. The physician's use of the drug for this extra-label use as part of the practice of medicine is not prohibited by law. *See Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration*, 37 Fed. Reg. 16,503, 16,503-04 (1972); Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1853-57 (1996). Under the 1997 drug reform law, for the first time the manufacturer can refer to scientific studies about the off-label uses under certain conditions. *See* § 402, 111 Stat. at 2365-66 (to be codified as amended at 21 U.S.C. ch. V, subch. E); *see also* discussion *infra* pt. III.D.2.a.

action by the FDA in practice only if there were express drug claims that could be attributed to the manufacturers.

### D. *The FDA's Renewed Scrutiny of Supplement Safety and Uses and the Congressional Response*

The FDA reviewed this policy in 1993 in the wake of the 38 deaths and 1500 adverse effects attributed to L-tryptophan, an amino acid sold as a dietary supplement and widely used and promoted for body-building.[61] Amino acids are the "individual structural units of proteins" and may be precursors for neurotransmitters and hormones.[62] The consumption of protein in foods ordinarily supplies sufficient amounts of amino acids.[63] In an Advance Notice of Proposed Rulemaking (FDA Advance Notice), the FDA described an FDA Task Force recommendation that amino acids be regulated as drugs because of information that their "primary intended use . . . is for therapeutic rather than nutritional purposes," and because of the "wide marketing" of these products for disease prevention and treatment purposes.[64] The FDA found that many amino acids clearly were being marketed in violation of the law because they were unapproved food additives.[65] The FDA invited comment on its intent to bring the amino acids into compliance with the law.[66]

The FDA also found that many herbs sold as supplements have "no known history of food use and, even without drug claims are used for medical purposes" and as traditional medicines.[67] The FDA indicated that its immediate goal was consumer safety, but also stated that "many herbal products are marketed for drug uses," and would be the subject of regulatory action based on the FDA's health fraud policy.[68]

The FDA also recognized an additional "other" category of supplements.[69] These included substances found in plant and animal products, such as fish oils and fibers, many of which have no nutritive value.[70] The FDA asked for comments on whether it should continue its policy of regulating these substances as foods.[71]

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61. *See* FDA Advance Notice, 58 Fed. Reg. at 33,695-66.
62. *Id.* at 33,695.
63. *Id.*
64. *Id.* at 33,697.
65. *Id.*
66. *Id.*
67. *Id.*
68. *Id.* at 33,698.
69. *See id.*
70. *See id.*
71. *See id.* at 33,699.

The FDA Advance Notice set off a controversy. Although the notice made some references to how the supplements were marketed and promoted, the FDA was seen as attempting to revive its earlier failed effort to classify high-dosage vitamins as drugs based upon widespread consumer use, in the absence of express drug claims by the manufacturer.[72] The application of the food additive provisions to amino acids, as suggested by the FDA Advance Notice, would effectively remove many of these supplements from stores, since "adequate scientific evidence to ensure" their safe use "did not exist . . . ."[73] A "national blackout day" was organized, and products that were the "target" of the FDA Advance Notice were "draped in black so that consumers could 'see' what would be taken away."[74] The FDA's Commissioner Kessler tried unsuccessfully to alleviate concerns by stating in Senate testimony that "any *nutritional* supplement currently on the market can be sold so long as it presents no safety problem."[75] The consumer reaction to the FDA Advance Notice had already "galvanized support" for the legislative efforts that led to DSHEA.[76]

### E. *Health Claims, Dietary Supplements, and the Enactment of DSHEA*

Another factor that contributed to the enactment of DSHEA was the FDA's 1994 decision that no dietary supplements then had the support needed to make health claims to help prevent disease, and that no lesser standard should be used for supplements than that applicable to conventional foods.[77] At one point, the FDA regarded any disease prevention claim on food to be a drug claim needing approval under the new drug procedures.[78] That policy changed when the FTC accepted the appropriateness of advertisements about the value of consuming high-fiber foods in preventing cancer, a value recognized by the National Cancer Institute (NCI).[79] The FDA started a rulemaking proceeding to determine the support needed by food manufacturers

72. *See* COMMISSION REPORT, *supra* note 16, at 13; *Mathews*, 557 F.2d at 325.

73. FDA Advance Notice, 58 Fed. Reg. at 33,697.

74. BASS & YOUNG, *supra* note 56, at 28.

75. *Legislative Issues Related to the Regulation of Dietary Supplements: Hearings of the Senate Comm. on Labor and Human Resources*, 103 CONG. 19 (1993) (emphasis added).

76. *See* BASS & YOUNG, *supra* note 56, at 7.

77. *See* 59 Fed. Reg. 395 (1994) (adding 21 C.F.R. § 101.4).

78. *See* HUTT & MERRILL, *supra* note 29, at 180.

79. *See* Peter B. Hutt, *Health Claims for Foods—An American Perspective*, Kellogg Nutrition Symposium, Toronto, Can. (Apr. 1986), *reprinted in* HUTT & MERRILL, *supra* note 29, at 183.

seeking to make health claims.[80] While the rulemaking proceeded, manufacturers continued to make health claims for products that engendered controversy. Congress resolved the debate by enacting the Nutrition Labeling and Education Act of 1990 (NLEA),[81] which authorized health claims for foods but required that such claims be based on well-designed studies and significant scientific agreement.[82] In addition, prior approval by the FDA was required in the form of a regulation governing the type of claim.[83]

Congress also authorized the FDA to establish a separate procedure and standard applicable to dietary supplements of nutritive value.[84] Notwithstanding this authorization to treat supplements differently, the FDA decided that the same standards should apply to health claims on both foods and dietary supplements. Under the standards, as applied by the FDA at that time, some conventional foods but no dietary supplements qualified to bear health claims on their labels.[85] The inability of dietary supplements, in practice, to meet the standard for health claims established in the NLEA for conventional foods contributed to the push that led to the enactment of DSHEA.

## III. IMPACT OF DSHEA AND EXPANDED OPPORTUNITIES FOR CLAIMS

DSHEA redrew the boundary between drug and dietary supplement claims, but that boundary is ambiguous on several points. DSHEA defined dietary supplements, gave manufacturers the right to make a new type of claim about the effects of the supplements, exempted certain publications from being regarded as labeling, exempted dietary supplements from being treated as food additives, and provided for re-examination of how health claims for supplements should be regulated. The more notable features of and issues concerning DSHEA are addressed below.

### A. *Health Claims*

#### 1. DSHEA Provisions

The DSHEA provisions on health claims are distinct from—but have influenced—the developments that led to DSHEA's provisions on other

80. *See* 52 Fed. Reg. 28,843 (1987).
81. *See* Pub. L. No. 101-535, 104 Stat. 2353 (1990) (adding 21 U.S.C. § 343(r)).
82. *See* 21 U.S.C. § 343(r)(3)(B)(i) (Supp. V 1993).
83. *See id.* § 343(r)(3)(A)(ii).
84. *See id.* § 343(r)(5)(D).
85. *See* BASS & YOUNG, *supra* note 56, at 15.

labeling claims.[86] While Congress was concerned about the inability of dietary supplements to qualify for health claims, Congress did not change the legal standard governing the claims for supplements. Instead, Congress directed the Commission created by DSHEA to consider the appropriate standard and report its recommendations with respect to the FDA regulations that determined that the same standards that apply to ordinary foods should apply to supplements.[87]

### 2. Commission Action and Analysis

After considering the matter, the Commission recommended that significant scientific agreement and regulatory approval by the FDA should apply to health claims on both dietary supplements and conventional foods.[88] Applying the same standard serves the interest of fairness in ensuring a level playing field and helps prevent consumer confusion.[89] Some supplements also have now qualified to bear health claims.[90]

The Commission recommended that the FDA permit more involvement by outside expert reviewers in the FDA review process without making the views of the experts presumptive.[91] Under this approach, the FDA is to identify the criteria for determining whether reviews by outside experts will be scientifically qualified, balanced, reliable, and independent.[92] Submissions from a panel meeting the criteria would

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86. *See* discussion *infra* pt. III.C.1.

87. *See* § 12, 108 Stat. at 4332-33. The FDA was required to issue regulations in response to any Commission recommendation for a regulatory change, and if the FDA did not act on a timely basis, dietary supplements would have been exempt from the requirements of the NLEA. *See id.*

88. *See* COMMISSION REPORT, *supra* note 16, at vii & 31.

89. *See id.* at 34. The need to have adequate testing of the supplement is illustrated by the results of a National Cancer Institute (NCI) study that had aimed to determine whether beta carotene supplements would reduce the risk of cancer in smokers because of the antioxidant qualities of the vitamin. *See* Gina Kolata, *Studies Find Beta Carotene, Used by Millions, Doesn't Forestall Cancer or Heart Disease*, N.Y. TIMES, Jan. 19, 1996, at A16. Those receiving the supplement actually had higher incidence of cancer, and the NCI ended the study before completion because of the possible adverse effects from the supplement. *See id.* This study indicates that the pill can, indeed, be different from the food, and that studies are needed on the supplement itself to determine its benefits.

90. *See* COMMISSION REPORT, *supra* note 16, at 33 tbl. 2 (Approved Health Claims for Dietary Supplements and Conventional Foods).

91. *See id.* at 35.

92. *See id.* at vii-viii & 35 (recommending that the FDA ensure broad input, including from scientists outside the agency and from other governmental agencies, to determine the degree of scientific agreement existing for each health claim). The development of appropriate criteria is an important and difficult task. *See* Margaret Gilhooley, *The Administrative Conference and the Progress of Food and Drug Reform*, 30 ARIZ. ST. L.J. 129 (forthcoming

strengthen the petition and expedite the review process. In recent legislation, Congress has provided for additional expert input by authorizing health claims for foods or supplements based on "an authoritative statement" of the National Academy of Sciences (NAS) or of a scientific health agency of the government, unless the FDA provides otherwise through rulemaking.[93]

There have been constitutional challenges to the statutory requirement for FDA approval of health claims. A time deadline for FDA action on final rules concerning health claims has been found to be necessary, but the regulatory scheme has otherwise not been found to be constitutionally infirm.[94]

### B. *Definition and Availability of Dietary Supplements*

#### 1. DSHEA Provisions

Congress has now defined "dietary supplement" as a product "intended to supplement the diet that . . . contains one or more of the following dietary ingredients: (A) a vitamin; (B) a mineral; (C) an herb or other botanical; (D) an amino acid; [or] (E) a dietary substance for use by man to supplement the diet by increasing the total dietary

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1998); Merrill, *supra* note 60, at 1858.

93. 21 U.S.C. § 343(r)(3)(C) (as added by § 303, 111 Stat. at 2350-51). There are provisions for making rules effective upon publication. 21 U.S.C. § 343(r)(7) (as added by § 301, 111 Stat. at 2350-51).

The Commission recommended only that the FDA give considerable weight to the recommendations of other government agencies in determining whether significant scientific agreement exists for a health claim. COMMISSION REPORT, *supra* note 16, at iv & 36.

An NAS report for a federal agency was recently found to be subject to the Federal Advisory Committee Act (FACA), 5 U.S.C.A. 2 § 5(b) (1994). *See* Animal Defense Fund, Inc. v. Shalala, 104 F.3d 424, 431 (D.C. Cir.), *cert. denied*, 118 S. Ct. 367 (1997). Congress has since provided that the FACA does not apply to the NAS, but for an agency to make use of the reports, there must be balance on the committees, safeguards against conflict of interest, and publication of the names of proposed members. *See* Nicholas Wade, *Science Advisers Retain Independence but Must Be More Open*, N.Y. TIMES, Nov. 16, 1997, at 23.

94. *See* National Council for Improved Health v. Shalala, 122 F.3d 878 (10th Cir. 1997) (finding lack of standing); Nutritional Health Alliance v. Shalala, 953 F. Supp. 526, 530 (S.D.N.Y. 1997).

intake. . . ."[95] The supplements are "deemed" foods, except when they are intended for a use covered by the drug definition.[96]

The new definition parallels the categories discussed in the FDA Advance Notice, and seems to be a reaction to the theories raised by the FDA about the factors that could lead to drug status. Indeed, Congress declared the Advance Notice to be "null and of no effect insofar as it relates to dietary supplements" and the FDA was directed to revoke the notice.[97]

The definition of supplements as "dietary" indicates that the supplements should have a biological basis, in the sense that they are derived from natural products (such as herbs and botanicals), are the same as substances found in foods (such as vitamins and minerals), or are physically needed substances derived from foods (such as amino acids).

### 2. Analysis

While dietary supplements have to be intended to supplement the diet, the meaning of "dietary" is not stated. In describing structure and function claims, DSHEA refers to both "dietary ingredients" and nutrients, indicating that supplements need not be nutrients.[98] In light of this provision, the definition and the statutory rejection of the Advance Notice, herbal supplements labeled simply as dietary supplements, without any disease-related labeling claims, should not be considered drugs merely because they contain nonnutritive ingredients, or lack a history of food use. Herbal supplements will be governed by the same demanding tests that have applied in establishing whether nutritive supplements are drugs.[99] Thus, any effort to show that herbs are drugs, based on objective factors, will depend upon establishing the level at which consumers use the product for a drug purpose rather than a "dietary" one. Congressional rejection of the FDA Advance Notice indicates a concern with the availability of supplements, and suggests

95. *See* § 3, 108 Stat. at 4327 (enacting as amended 21 U.S.C. § 321(ff)). By definition, a dietary supplement cannot include a substance that is the subject of a new drug application or an investigational new drug application, without the FDA's permission. *Id.* As a result, a botanical version of an approved drug, such as Taxol, could not be sold as a supplement without FDA permission. *See* Robert G. Pinco & Paul D. Rubin, *Ambiguities of the Dietary Supplement Health and Education Act of 1994*, 51 FOOD & DRUG L.J. 383 (1996) (discussing uncertainties concerning whether a hormone, such as melatonin, is a dietary substance).

96. *See id.*

97. § 11, 108 Stat. at 4331.

98. *See* 21 U.S.C. § 343(r)(6); discussion *infra* pt. III.C.

99. *See* discussion *supra* pt. II.B. The Commission recognized that, under DSHEA, botanical products should continue to be marketed as dietary supplements when properly labeled. COMMISSION REPORT, *supra* note 16, at 57.

that a strong showing is needed to establish drug intent in the absence of express manufacturer's claims.[100] Congress did not expressly alter the tests for determining drug intent, though, and the objective test for determining a manufacturer's intent presumably remains a potential basis for determining intent, but one that is difficult to satisfy.

To meet the demanding showing, the agency could seek to show that consumers use a supplement solely for drug purposes. The sale of bear parts as a "dietary supplement" without any other claims might provide an example of such an extreme case, given the use of bear gall and other parts in traditional medicine.[101] Widespread consumer use would have to be particularly strong to outweigh the dietary use if it is to be considered sufficient to establish the manufacturer's intent in the absence of other factors.

The expansive approach to the basis for determining a manufacturer's intent, upheld in the litigation over the FDA's rule regulating tobacco,[102] provides support for giving consumer use greater effect in determining the manufacturer's intent concerning the use of certain types of products. Tobacco products contain nicotine, which has a discernible physical effect, that is addictive. This effect makes it possible to show that manufacturers can reasonably foresee that consumers will recognize and use the product for its drug effects. Some supplements can have marked physical effects, such as high doses of stimulants, anti-depressives or substitutes for narcotic-type drugs, like herbal ecstasy. Through use, the consumers can recognize the effects of the supplements as ones that relate to disease or drug-like effects, even if the use is not addictive. In these situations, there is a similar basis for maintaining that the manufacturer should foresee that consumers will recognize the effects through experience and use products containing potent doses as a drug even when the use is not stated on the label.

A different question arises when a manufacturer of a dietary supplement makes an express claim. The claim itself may suggest use to prevent or treat disease or a non-dietary use and needs careful examination.[103]

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100. *See* discussion *supra* pts. II.D. & III.A.1.

101. *See* Tom Johnson, *Senate Moves to Shield Wildlife from the Claws of Poachers*, THE STAR-LEDGER, Mar. 11, 1997, at 1 ("Bears are highly sought as aphrodisiacs or tonics in Asian medicinal shops, where their gall bladders fetch as much as $1,000 each.").

102. *See* Coyne Beahm, Inc. v. FDA, 966 F. Supp. 1374 (M.D.N.C. 1997). The FDA rules are in 61 Fed. Reg. 44,396 (1996) (to be codified at 21 C.F.R. pt. 897).

103. *See* discussion *infra* pt. III.C.2.b.ii.

### C. *Statements of Nutritional Support and Structure/Function Claims*

#### 1. DSHEA Provisions and Scope

DSHEA provides an important new opportunity for dietary supplements to make "statements of nutritional support"—the title for this section of DSHEA when enacted—without the claim being considered a drug claim.[104] These statements can describe "the role of a nutrient or dietary ingredient intended to affect the structure or function in humans," or describe "general well-being from consumption of a nutrient or dietary ingredient."[105]

DSHEA imposes some significant limits on these statements. The statements must be substantiated and cannot be misleading. The products must also bear 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."[106] The list parallels the drug definition.[107]

Some of those involved in the legislative debate over DSHEA apparently viewed the authorization of statements of nutritional support as a "trade-off" under which NLEA was left in place to regulate health claims concerning the relationship between disease and foods and nutritive supplements. In return, structure and function claims could be made for dietary supplements, without the supplements being subject to the drug law, even if the effects were not those of a nutrient.[108]

To understand how structure and function claims have expanded the ability to make drug claims, some background is needed about the scope of the drug definition and the traditional boundaries between foods and drugs. An article can be a drug not only because its label makes disease prevention and treatment claims, but also because it claims to affect the structure and function of the body, such as by helping to reduce weight.[109] Foods have always been statutorily excluded from this provision, since otherwise their very effect in providing sustenance

104. *See* § 6, 108 Stat. at 4329.

105. 21 U.S.C. § 343(r)(6). The statements also can relate to classical nutrient deficiency disease, but the "structure or function" claims are the most important and far-reaching in their potential scope.

106. 21 U.S.C. § 343(r)(6)(C).

107. *See* 21 U.S.C. § 321(g) (1994) (stating that a drug means articles "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease."). The two most important categories, drug prevention and treatment, are used as shorthand in this Article to refer to the various uses that establish a disease claim.

108. *See* BASS & YOUNG, *supra* note 56, at 53, 55.

109. *See* 21 U.S.C. § 321(g).

would make them drugs. To gain the benefit of this exclusion from the drug testing requirements, some unconventional products have claimed to be foods, leading to the need for court determinations of what makes something a food.

A leading case interpreted the food definition on a "common sense" basis as covering articles primarily used for "taste, aroma, or nutritive value."[110] A product sold as a "starch blocker" was a drug rather than a food under this test, as it was claimed to block digestion to prevent weight gain, a use that did not provide nutrition.[111]

DSHEA now authorizes "statements of nutritional support" on dietary supplements for both nutrients and "*dietary* ingredients," and exempts the statements from the drug provisions.[112] Claims are, thus, now exempt from the drug provisions not only when they relate to substances of nutritive value, but also when they are "dietary" in some other sense. Moreover, the definition of dietary supplements in DSHEA encompasses herbs and botanicals and other "dietary" substances, some of which may have no history of food use. The potential reach of structure and function claims becomes clearer when one considers that many claims recognized by the FDA as OTC drug claims are structure and function claims rather than disease claims. Thus, the OTC review covers claims for sedatives, stimulants, laxatives, some contraceptive products, and miscellaneous products, a category broad enough to include aphrodisiacs.[113]

As a result of the authorization of structure and function claims in DSHEA, an increased number of claims are being made for supplements, particularly herbal supplements, that would not have qualified for exemption from the drug provisions under the earlier judicial test. The FDA has been notified of over 1000 such claims, including that ginkoba "improves memory and concentration" and "enhanc[es] your mental focus," that saw palmetto "maintain[s] prostate health and well-being," that milk thistle "nutritionally supports healthy liver function," that echinacea "helps promote general well-being during the cold and flu season" and "supports healthy immune function," that ginseng provides "stress support" and "gives active adults a competitive edge," that

110. *See* Nutrilab, Inc. v. Schweiker, 713 F.2d 335, 338 (7th Cir. 1983). Because the test focused on the primary use of the substance, coffee and prunes were not considered drugs because of the occasional consumer use to affect bodily functions. *See id.*

Another court considered claims about lipotropic properties to be drug claims. *See* United States v. Vitasafe Formula M, 226 F. Supp. 266, 278 (D.N.J. 1964).

111. *See id.* at 338-39.

112. *See* 21 U.S.C. § 321(g); 21 U.S.C. § 343(r)(6) (emphasis added). The term "statements of nutritional support" was used as the heading in the statute as enacted. § 6, 108 Stat. at 4329.

113. *See* 21 C.F.R. § 330.05 (1997).

melatonin is "produced in the pineal gland . . . and aids in the regulation of circadian rhythms," and that valerian "Night Time" has substances in the root that "slow the central nervous system activity which can be helpful in the evening."[114]

The FDA has not taken a position on many claims for which it has received notices, but this does not necessarily indicate concurrence.[115] When the FDA does object to a claim, the manufacturers may revise their claims to make more general statements of well-being, or claims for general support of bodily functions. Thus, there may be a continual generation of claims that test the scope of permissible statements of nutritional support. The FDA also has recognized that there are gray areas where it is unclear whether claims are appropriate structure and function claims or whether they are drug claims.[116] While there is a need for further guidance concerning the line between nutritional support claims and inappropriate drug claims, providing guidance with respect to these matters is a daunting task.

### 2. Analysis

Congress has enacted an enigma in this provision of DSHEA. Statements of "nutritional" support are now permitted concerning the effects of "dietary" ingredients on the structure and function of the body, even though the ingredients are not nutrients, and lack the other characteristics of taste and aroma used in the past to identify foods. At the same time Congress has failed to identify what makes something a "dietary" ingredient. Conceivably, at one extreme, one might think Congress intended "dietary" to include any biological substance that can be ingested, and that statements of nutritional support can cover any non-therapeutic effect the substance may have. If so, Congress gave "dietary" a meaning beyond its normal one since the dictionary definition of dietary reflects a "food" meaning.[117] If Congress intended

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114. *See Dietary Supplement Statements of Nutritional Support*, THE TAN SHEET, Jan. 15, 1996, at 11-15. Under 21 U.S.C. § 343(r)(6), the FDA must be notified of such statements, but no prior approval by the FDA is needed.

115. *See Labeling: Current Issues and Policy Decisions*, 39th Annual Educational Conference, Food and Drug Law Institute (Dec. 12, 1995) (speech by F. Edward Scarbrough).

116. *See id.*

117. Webster's Dictionary defines "dietary" as "of or related to a diet," and "diet" as "food and drink regularly provided or consumed." WEBSTER'S THIRD NEW INTERNATIONAL DICTIONARY 629 (1963); *see Proposed Rule, Dietary Supplements Containing Ephedrine Alkaloids*, 62 Fed. Reg. 30,678, 30,699 (1997) [hereinafter *Proposed Rule, Dietary Supplements*]; *infra* pt. III.C.2.b. for discussion of the FDA's interpretation of "dietary" based on dictionary definitions of "food." The FDA cited Webster's Dictionary definition of "diet" as " 'an organism's usual food and drink' " and Dorland's Medical Dictionary definition as "'the

a narrower meaning, it did not indicate what the parameters were apart from the word "dietary" itself. There is virtually no legislative history.[118] The interpretation of DSHEA, thus, presents a challenge.[119]

Determining what dietary claims are appropriate involves considering interrelated factors about what makes a claim a disease claim, a dietary claim, or a prescription claim. Since statements of nutritional support cannot by law be disease claims, identifying disease claims is a critical first step in analysis.

### a. Identifying Disease Claims

While DSHEA precludes disease claims on supplements, there is debate about what constitutes a disease claim. Some believe that only express claims are barred, and that implied disease claims are permissible because of congressional concern with health promotion, as expressed in the findings for DSHEA.[120] On the other hand, the drug provisions have long applied to implied disease claims that would "create in the mind of the public" the idea that a product can be used for disease prevention or treatment.[121] A claim that a supplement would "promote non-suicidal feelings" should be regarded as a claim to prevent or treat depression even if the word "depression" were not mentioned. The health needs of the public can be adversely affected if products can imply usefulness in forestalling disease when the products

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customary allowance of food and drink taken by any person from day-to-day. . . .' " 62 Fed. Reg. at 30,699. According to the FDA these definitions suggest that "diet is composed of usual food and drink that may be designed to meet specific nutritional requirements." *Id.*

118. *See* 140 CONG. REC. H1180 (daily ed. Oct. 6, 1994) (Statement of Agreement); 140 CONG. REC. S14801 (daily ed. Oct. 7, 1994). The Statement specifies that it is "the entire legislative history for DSHEA." *Id.*

119. Statutory interpretation is to begin with the text of the statute as the primary source for determining Congress' intent. *See* Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc., 467 U.S. 837, 842-43, *reh'g denied*, 468 U.S. 1227 (1984). In the absence of clear congressional intent, the courts will defer to a reasonable agency interpretation. *See id.* at 843-44. The Supreme Court will, at times, consider other sources in determining congressional intent, including the legislative history, the statutory framework, and the purpose of the statute. *See* Babbitt v. Sweet Home Chapter, 515 U.S. 687, 708 (1995).

120. *See* COMMISSION REPORT, *supra* note 16, at 36; § 2, 108 Stat. at 4325-26 (finding that "the importance of nutrition and the benefits of dietary supplements to health promotion and disease prevention have been documented increasingly"). Some members suggested that a claim that a supplement would affect immune function or resistance should be a "legitimate" claim of nutritional support, notwithstanding that the FDA has historically been sensitive that claims relating to immune function imply use in the treatment of AIDS. *See* COMMISSION REPORT, *supra* note 16, at 36.

121. United States v. Fairfax Cigarettes, 113 F. Supp. 336, 338 (D.N.J. 1953); *see* United States v. 'Line Away Temporary Wrinkle Smoother, Coty', 415 F.2d 369, 372 (3d Cir. 1969) (finding that implied claims that a product was a pharmaceutical made the product a drug).

do not have the level of support and review ordinarily required for drugs.

Once it is accepted that implied disease claims are not permissible, there can still be difficulties in determining when a claim is sufficient to constitute an implied disease claim. Claims for supplements often take the form of a statement that the supplement promotes or supports the health of an organ of the body, without expressly stating that the supplement helps prevent the organ from becoming diseased.

The Commission report recognized a difference between claims to correct a function and claims to maintain a function.[122] Under this guidance, statements to "restore" a normal, or "correct" an abnormal, function of the body should not be made when they relate to an abnormality that suggests the presence of disease, such as a claim to "restore" normal blood pressure when the abnormality implies hypertension.[123] Claims to maintain or support a body system, organ or function can be appropriate, depending upon the context, when the statement does not suggest disease prevention or treatment or use for a serious health condition beyond the ability of the consumer to evaluate.[124] In the report, some Commission members indicated they were "troubled" by references to specific organs, and found the "most problematic" wording relates to references to organs such as the heart, liver, or prostate, which are "associated with major clinical conditions."[125]

On analysis, the factors discussed in the Commission report indicate the relevance of the need for medical advice in helping to identify an inappropriate supplement claim and a disease-related claim. A claim to stimulate or maintain heart function is an example of a claim beyond the role of the consumer to evaluate, and one that calls for medical advice. Such claims are more likely to be viewed by the users as related to disease.

The FDA has taken the position in connection with "herbal fen phen" products that they are unapproved drugs because the name and claims reflect that they are intended for the same use as prescription drugs which have been withdrawn from sale because of safety concerns.[126] Claims for substitutes for prescription drugs are particularly

122. *See* COMMISSION REPORT, *supra* note 16, at viii, 38-39.

123. *See id.*

124. *See id.*

125. *See id.* at 36-37.

126. *See FDA Warns Against Drug Promotion of "Herbal Fen-Phen,"* FDA TALK PAPER, T97-56 (Nov. 6, 1997), available at http://www.fda.gov/bbs/topics/ANSWERS/ANS00832.html; *FDA Warns Consumers About Herbal Weight Loss Mixtures*, N.Y. TIMES, Nov. 7, 1997, at A19 (" It is illegal . . . to call this product something that is exactly like a medication and to make medical claims that it will cause weight loss and treat obesity, like the prescription products

troubling because they are likely to involve effects or conditions beyond the ability of the consumer to evaluate.[127] While non-prescription claims also can be disease claims, the need for medical advice and a prescription can be especially useful in identifying implied disease claims.[128]

A claim to lower high blood cholesterol levels, not through diet but through use of an isolated ingredient, provides another example of a use for which medical advice has been considered necessary and one that can imply a medical use to consumers.[129]

### b. Identifying "Dietary" Claims

#### i. Health Promotion and Preclusion of Herbal Ecstasy

The FDA maintains that, under the definition, dietary supplements are intended to supplement the diet, and that the congressional findings in DSHEA suggest that Congress intended supplements "to augment the diet to promote health and reduce the risk of disease."[130] Accordingly, claims for recreational effects, such as being a substitute for illicit street

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do"); "Cholesterol-Lowering Drugs 'Should Not Be Sold OTC' in the U.S., FDA states," THE PINK SHEET, T&G 7, Oct. 13, 1997.

127. *See, e.g.*, Sandra G. Boodman, *Now That Two Popular Weight-Loss Drugs Are Off the Market, What's Left for Dieters?*, WASH. POST, Sept. 16, 1997, at Z12 (reporting that some "programs are touting their use of so-called 'herbal' or 'natural' fen/phen," made up of ephedra and St. John's wort, a supplement popular in Europe for treating mild depression).

128. *See* discussion *infra* pt. III.2.c.

129. *See FDA Seeks Pharmanex Citizen Petition Request,* THE TAN SHEET, Oct. 13, 1997, at 1 (FDA letter finding claims that Cholestin reduces cholesterol levels to be disease claims). The issue also tests the scope of the definition of "dietary supplements" and its exclusion of articles covered by a new drug application (NDA) absent an FDA exemption. *See* 21 U.S.C. § 321(ff)(3). Cholestin contains an ingredient like that in a prescription drug which has an approved NDA. *See Cholestin "Designed to Be Different from Red Yeast Rice Merck Argues in Comments*, THE TAN SHEET, Feb. 9, 1998, at 17 (Merck maintains the product is "designed as . . . a generic alternative to Mevacor."). In a letter, the FDA has found that the product is a drug, and that it would "not be fair" to the NDA-holder if differences in purity and inactive ingredients made the product a dietary supplement. *See Lovastin Content Renders 'Cholestin' an Unapproved New Drug*, THE PINK SHEET, T&G 8, Oct. 13, 1997.

Some Commission members indicated that well-crafted claims relating to cholesterol levels would, in their view, be appropriate structure and function claims. *See* COMMISSION REPORT, *supra* note 16, at 37.

130. *Proposed Rule, Dietary Supplements*, 62 Fed. Reg. at 30,678; 21 C.F.R. pt. 111 (1997); *see also Committee Reviews Evidence that Ephedra Is More Drug than Food or Dietary Supplement*, FOOD CHEMICAL NEWS, Sept. 9, 1996, at 9-10 (statement of Food Advisory Committee Meeting, Aug. 27, 1996) (" 'In China, [ephedra] is always used to treat diseases, not as a food. . . . This does not have any value in terms of diet.").

drugs, are drug claims, and not claims to supplement the diet. The FDA relied on the common sense meaning of "diet" as well as the dictionary definitions that relate to "customary" or "usual" uses of food and drink.[131] This approach recognizes the need for a dietary connection for dietary supplements, links it to health factors and disease risk reduction, and excludes supplements that claim narcotic-like effects, such as herbal "ecstasy." The FDA did not indicate how to identify disease risk reduction factors without implying disease prevention. Presumably, it relates to the generality of the dietary claim, and the identification of a physical effect without suggesting disease prevention.

### ii. Statements of Nutritional Support: The Need for a Dietary Relationship and Food Analogy

When supplements make statements of nutritional support, which are exempt from drug regulation, it is important to look carefully at what makes the ingredient a "dietary" ingredient. Clearly, statements of nutritional support are *not* limited to the effects of nutrients since the statements can be made both for nutrients and dietary ingredients. The term "dietary" suggests, however, some analogy to food use and the effects consumers expect from foods in the diet.[132] If this approach is correct, claims that a dietary supplement provides a food-like energy boost, provides a wake-up effect like coffee, soothes to sleep like warm milk, or "promotes regularity" like fruits, would be appropriate. Such food analogies are clear enough that consumers can understand the context and types of effects to be expected. These claims are dietary in the sense that the supplement is represented as a food substitute—as a substitute source for the types of effects produced by ordinary foods in the diet.

Claims that substances not found in foods achieve effects not usually associated with foods should not be considered dietary claims merely because the claims are not disease claims. If balsa wood were shredded and put in a gelatin capsule, it would not be an appropriate statement of nutritional support to say that the product is an "internal swim aid" to help flotation.[133] To view such a claim as "dietary" expands the term to cover the non-therapeutic effects of any biological substance whenever the product is verbally described as having the effect of a

131. *See Proposed Rule, Dietary Supplements*, 62 Fed. Reg. at 30,699; *supra* note 117.

132. *See* COMMISSION REPORT, *supra* note 16, at 38 (statement of the author that an appropriate statement of nutritional support "would need to identify a dietary relationship for the supplement").

133. *See generally* THOR HEYERDAHL, KON-TIKI (1957) (discussing the buoyant nature of balsa wood).

dietary ingredient. While a claim as a swim aid would presumably be precluded by the FDA's position that dietary claims have to relate to health promotion, the need to have an analogy to a food use has a separate focus.[134] Thus, claims that a substance from a tree improves memory and enhances mental focus or prevents aging (or, for that matter, improves intelligence or makes one think better) have no food or diet parallels.[135] Claims that a supplement may be used as an oral contraceptive similarly would be inappropriate. Contraception is not itself a disease claim but it relates to the structure and function of the body. It would be absurd to believe that Congress intended such a claim to qualify as a "statement of nutritional support."

What constitutes a food- and diet-related use under this approach depends primarily upon the claim. The test is claim-specific and relates to whether a consumer would be able to understand how the supplement is to be used to obtain effects normally associated with the use of foods. The source of the supplement is a relevant but not a dispositive factor. If the ingredient comes from a food source, the claims are more likely to be understood by the consumer as diet-related.

This theory for limiting structure and function claims is not without its difficulties. Using the term "dietary ingredient" to limit statements of nutritional support could be seen as inconsistent with the broad definitional scope of "dietary supplements" discussed above.[136] The definitional section and the statements of nutritional support are separate, however. Even if a statement of nutritional support cannot be made, the substance can continue to be sold with simply the claim that it is a dietary supplement, when it does not make disease or non-dietary claims and there is no other basis for finding that the product is intended to be a drug. Allowing sale when the only claim is as a dietary supplement is consistent with congressional concern that consumers have access to dietary supplements for dietary purposes even if these are not recognized nutritional uses.

When a manufacturer makes a more specific claim about the dietary effects of a supplement, different issues arise. The manufacturer who promotes a supplement for a specific "dietary" use to the public-at-large has a greater responsibility to make a claim that gives "dietary" an understandable meaning. The requirement of substantiation for state-

134. *See supra* note 126 and accompanying text; discussion pt. III.C.2.b.

135. Claims of improved memory may also indirectly suggest a usefulness in treating the effects of Alzheimer's Disease. There have been some short-term studies that have shown some improvement in some patients, but the results are preliminary. *See* Transcript, *World News Tonight with Peter Jennings* (ABC television broadcast, Feb. 6, 1997).

136. *See* discussion *supra* pt. III.B.2.

ments of nutritional support indicates that Congress had greater concern about the validity of these claims. In addition, Congress used the title "statements of nutritional support" for claims concerning nutrients and "dietary" ingredients, thus indicating the need for some connection between the claim and the diet.[137]

At a minimum, statements of nutritional support for a dietary supplement should expressly indicate that the supplement has a "dietary" role. The label claims should specify that the supplement achieves its effect through "dietary support," "dietary promotion," or in other terms that expressly identify the role as a "dietary" one. An express dietary reference serves to differentiate the effects of supplements from those of drugs. The manufacturers who make the claims also should have the burden of convincing the public that the role is a "dietary" one—a burden that may be difficult for unfamiliar ingredients.

### c. "Dietary" and Need for Professional Advice

Another meaning that can be inferred from the term "dietary" is that claims should not refer to uses that require professional supervision and a prescription.[138] A drug can require a prescription because of its toxicity or because of the need for diagnosis to treat a more serious condition.[139]

Dietary ingredients, like foods, should be within the ability of a consumer to use without medical supervision. As the Commission recognized, a claim of effectiveness for prescription drug claims, such as use as an oral contraceptive would be inappropriate for a "dietary supplement," even assuming the supplement were effective for this purpose.[140]

The principle that dietary supplements should not claim prescription uses that need medical supervision represents an important aspect of the

137. The NLEA requires FDA approval for claims concerning disease and "health-related conditions" for conventional foods and for dietary supplements that are nutritive. *See* 21 U.S.C. §§ 343(r)(1), 343(r)(5)(D). When a nutritive supplement makes disease claims, the FDA may possibly regard the claim as an unauthorized health claim rather than an unauthorized drug claim. The NLEA also applies to claims about "health-related conditions." *See id.* This independent requirement of the NLEA could impose limits on "structure or function claims" for dietary supplements and conventional foods even when the claims are not sufficient to be disease claims. In other words, the NLEA has a coverage that goes beyond disease claims and encompasses abnormal health conditions that can lead to disease.

138. A drug is limited to prescription status when it is not safe for use except under professional supervision because of "its toxicity, other the method of its use, or the collateral measures necessary to its use." 21 U.S.C. § 353(b)(1)(B) (1994).

139. *See* United States v. 'Decholin', 264 F. Supp. 473, 479-80 (E.D. Mich. 1967).

140. *See* COMMISSION REPORT, *supra* note 16, at 37.

boundary between dietary supplements and drug claims. The need for a prescription helps both to indicate that a claim is a disease-related claim and that a claim is not a dietary claim. The Commission also recognized that nutritional support claims should not relate to matters beyond the ability of the consumer to evaluate.[141]

There may be debate with respect to some products whether professional diagnosis and supervision is needed, and additional attention will have to be given to the factors that necessitate prescription limitations.[142] The principle is, though, an important one in establishing some discernible boundaries to protect consumers from inappropriate claims.

### 3. Substantiation for Statements of Nutritional Support

Additionally, statements of nutritional support must be substantiated and cannot be misleading.[143] This is an important requirement that may preclude many claims. The FDA may directly challenge dietary supplement claims that make express or implied disease claims as inappropriate dietary supplement claims. For non-disease claims in a gray area, the difficulties in litigating the issue of what is a "dietary" claim may lead the agency to emphasize, as an enforcement priority, whether there is adequate substantiation for the claim. The adequacy of the substantiation for the claim may, in practice, be a more important focus for enforcement and regulation than the difficult definitional issues. Manufacturers may simply not be able to prove the vaguer claims, and extensive and expensive research may be necessary for claims that relate to preventative or moderate effects.[144]

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141. *See id.* at viii & 38-39.

142. *See generally 'Decholin,'* 264 F. Supp. at 473 (illustrating various factors necessitating prescription limitations). In recent years, the prescription status of drugs has generally been determined administratively—often without court litigation. *See* HUTT & MERRILL, *supra* note 29, at 416 n.2.

143. *See* 21 U.S.C. § 343(r)(6).

144. *See* COMMISSION REPORT, *supra* note 16, at 69 ("A statement that a product provides a feeling of well-being may be confounded with the placebo effect, thus double-blind studies using placebo would be essential to assessing such statements,"); *see id.* at 70 ("Determination of prevention in the general population, or even in a population at risk for developing a specific disease, is more expensive and difficult than determination of an effect in a population with a disease."); *see id.* at 69-70 ("Many dietary supplements claim to improve or optimize the functioning of the human body and do not result in immediate drug-like effects. The 'soft' end points of research supporting such claims can make clinical research results ambiguous. The cost of research to prove moderate benefits is significantly higher than that of research to prove immediate relief of disease symptoms."); *see id.* at 69 ("A statement that a product enhances immune function requires an appropriate challenge. . . .").

How demanding the substantiation requirement is depends, though, upon the type of support needed to meet it. The Commission considered the various factors that have been considered by the FTC in dealing with the substantiation of advertising claims. The type of benefit claimed, the difficulty of doing tests, and the amount of substantiation that experts in the field consider reasonable affect the type of testing and support necessary for general advertising claims.[145] For unqualified health claims, the level of support among scientists that experts find necessary is key.[146] The Commission found that the "substantiation for statements of nutritional support will likewise vary depending on the nature of the statement being made, the health importance of the statement, and the difficulty of conducting experimental studies."[147] These factors suggest that significant agreement among scientists would be needed for the statements of nutritional support that relate to conditions of health importance, and that depend on difficult long-term testing.[148] For significant scientific agreement to exist, scientists would need to know about the information. Thus, the relevant studies and scientific information would need to be available to the scientific community, and, in effect, be public. The public availability, when needed, also would help alleviate the enforcement difficulties in determining whether the claims have been adequately substantiated.

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145. *FTC Policy Statement on Advertising Substantiation*, 48 Fed. Reg. 10,471 (1984), *reprinted in* Thompson Medical Co., 104 F.T.C. 648, 839(1984), *aff'd*, Thompson Medical Co. v. F.T.C., 791 F.2d 189 (D.C. Cir. 1986), *cert. denied*, 479 U.S. 1086 (1987); *FTC Enforcement Policy Statement on Food Advertising*, 59 Fed. Reg. 28,388, 28,393 (1994). *See generally* C. Lee Peeler & Susan Cohen, *The Federal Trade Commission's Regulation of Advertising Claims for Dietary Supplements*, 50 FOOD & DRUG L.J. 349 (1995) (discussing the "application of the Commission's regulatory approach to dietary supplements").

146. *FTC Enforcement Policy Statement on Food Advertising*, 59 Fed. Reg. at 28,393. The FTC "regards the significant 'scientific agreement standard' . . . to be the principal guide" to the support needed for advertisements about health claims on the relationship between food and disease. *Id.* at 28,393.

147. COMMISSION REPORT, *supra* note 16, at 43.

148. The factors that influence scientists when there are difficulties in conducting tests is also indicated in a report of the National Research Council (NRC) upon which the FDA relied in developing its regulations on health claims. *See Diet and Health: Implications for Reducing Chronic Disease Risk*, Committee on Diet and Health, Food and Nutrition Board, Commission on Life Sciences, National Research Council, at 23 (1989). The NRC Committee on Diet and Health recognized that direct studies of the causal effect of a dietary substance on health and chronic diseases is often not possible. *See id.* at 23. The committee looked to other types of studies, and the "strength, consistency, and preponderance of data and the degree of concordance in epidemiologic, clinical, and laboratory evidence" in determining the strength of the evidence that supported the recommendations made by the panel with respect to health claims and food. *Id.* at 38; *see also* COMMISSION REPORT, *supra* note 16, at 31.

Some Commission members believed that historical use would be recognized by experts as sufficient substantiation in the case of a qualified claim that relied on historical use as support.[149] Another assessment is that experts still would want scientific support for substantiation in the case of claims that have health importance.[150] DSHEA imposes an affirmative substantiation obligation for statements of nutritional support, and not simply a disclosure obligation about any inadequacies in the substantiation. Moreover, even if a claim is qualified, there can still be the potential to mislead consumers unless a qualified claim fully indicates the existence of any controversy among experts, and any inconsistency of the claim with the larger body of evidence.[151]

To make this substantiation obligation a meaningful one, the FDA has to be able to obtain access to the files of the manufacturer to determine whether the manufacturer has affirmatively developed support for the claims made. The FDA, however, does not have the subpoena powers that the FTC has. While the FDA can inspect the documentary records of manufacturers of new drugs, the FDA has no express authority to inspect the records of food or supplement manufacturers.[152] Without that authority, it may be difficult to enforce the substantiation obligation with respect to labeling claims.[153] If the manufacturer relies on studies that are not public, there is an especially great need for access to private files to ensure that there is substantiation. While the FDA can take enforcement action if it can affirmatively show that there has been a failure of substantiation, the need to make this type of showing is difficult and essentially shifts away from the manufacturer the need to develop adequate support. The FDA should test its authority under the existing law to require manufacturers, by regulation, to make records available when there is a need for access.[154] If that regulatory

149. *See* COMMISSION REPORT, *supra* note 16, at ix-x & 43-44.

150. *Id.* (statement of individual member of the Commission).

151. *See id.*; *FTC Enforcement Policy Statement on Food Advertising*, 59 Fed. Reg. at 28,394.

152. *See* 21 U.S.C. § 374 (1994). With respect to the FTC's investigative powers, see 15 U.S.C. § 49 (1994); *Antitrust Law Developments*, A.B.A. ANTITRUST L. SEC. REP. ch. VII (1997).

153. *See* BASS & YOUNG, *supra* note 56, at 57.

154. *See Food Labeling; Nutrient Content Claims and Health Claims; Special Requirements*, 61 Fed. Reg. 3885 (1996) (proposed rule to be codified at 21 C.F.R. pt. 101). The FDA authority is disputed and rests on a theory raised in the 1960s but found not ripe for review apart from a particular dispute. *See, e.g.*, Toilet Goods Ass'n v. Gardner, 387 U.S. 167 (1967); *see also* COMMISSION REPORT, *supra* note 16, at x & 44 (individual statement that the FDA should have access to files to substantiate safety and statements of nutritional support through this type of rule or through legislative action if necessary).

authority is not recognized, Congress should provide adequate authority by legislation.

### D. *Labeling Exemption for "Publications"*

#### 1. DSHEA Provisions

DSHEA created an important exemption, with uncertain bounds, for a "publication" that is used "in connection with sale," even though the publication may contain information about therapeutic uses of supplements.[155] An exempted "publication" is not considered "labeling" subject to the requirements of the FFDCA.[156] A book or other writing that relates to the drug uses of a product only becomes subject to FDA regulation when the written material "accompanies" a product or is used as part of an integrated scheme to promote the product at the time of sale.[157] Labeling subject to the FFDCA cannot contain disease or other drug claims without meeting the obligations for testing and pre-market approval applicable to drugs.[158] By allowing manufacturers and sellers of supplements to make available to consumers exempted "publications," DSHEA opens up the possibility of promotion of the supplement for use by consumers for disease purposes that the manufacturer would not be able to claim on the labeling itself.

Only certain publications are exempt, but determining the exact scope of the exemption presents issues. The law refers to a "publication, including an article, a chapter in a book, or an official abstract of a peer-reviewed scientific publication that appears in an article and was prepared by the author or the editors of the publication, which is reprinted in its entirety. . . ."[159] The sparse official legislative history for DSHEA specifically states that the exemption "does not apply to a summary of a publication other than an official abstract of a peer-reviewed scientific publication."[160]

To qualify for the exemption, the publication cannot be misleading and must be displayed or presented, or be displayed with such other items on the same subject matter as to present a "balanced view" of the

155. *See* 21 U.S.C. § 343-2 (1994).

156. *Id.* No exemption is made in DSHEA with respect to the FTC's jurisdiction over advertisements that are misleading. *See* 15 U.S.C. §§ 45, 52 & 55 (1994).

157. *See* discussion *supra* pt. II.A.

158. *See* 21 U.S.C. § 343-2.

159. *Id.*

160. *See* 140 CONG. REC. H1180 (daily ed. Oct. 6, 1994) (Statement of Agreement); 140 CONG. REC. S14,801 (daily ed. Oct. 7, 1994). The Statement specifies that it is "the entire legislative history for DSHEA."

available scientific information.[161] The publication cannot promote a particular manufacturer or brand, and the displays in a retail store have to be physically separate from the supplements, and not contain appended stickers.[162]

### 2. Analysis

#### a. Scope of Exemption

The Commission report discussed the difficult issues in determining the scope of the publication exemption. One possible interpretation could be that the term "publication" is limited only to publications directed to the scientific community, and not to consumer-directed material. The Commission found that the emphasis in the statute on reprinting a publication "in its entirety," "the care given to describing an official abstract of a scientific publication," and the legislative history on summaries "all suggest that Congress was referring primarily to scientific publications."[163] Nonetheless, the Commission recognized that the term "publication" has a broader meaning, and would "appear" to apply to almost any publication about scientific information.[164] The legislative history indicates that the exemption applies only to summaries that are official abstracts of articles, but scientific articles can be review articles that contain summaries of various studies, and these would also seem to be publications under this provision.

Another limitation clearly has merit. Specifically, an exempted publication "should be independent and should not be written, developed, or funded by the manufacturers or sellers of dietary supplements."[165] Further, the writing of the publications should not be financed by the sellers (apart from any support provided for the underlying scientific research). The provision on abstracts clearly reflects a concern with independence, and the references to book chapters and articles is also consistent with having a distinct author. The

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161. 21 U.S.C. § 343-2.

162. *Id.*

163. COMMISSION REPORT, *supra* note 16, at 46.

164. *Id.* at xi & 47. The provision still can be considered ambiguous *because* the statutory reference to peer-reviewed scientific publications indicates the type of publication to which the provision applies, and there would have been no reason to refer specifically to such publications if the exemption was meant to be open-ended.

*But see* BASS & YOUNG, *supra* note 56, at 51-52 (expressing the view that the provision is not limited to "third party literature," and that a publication can itself be a summary of the literature).

165. COMMISSION REPORT, *supra* note 16, at 47 (stating the individual view of one of the Commission members).

provision that the publication be reprinted "in its entirety" makes sense only if the publication is written by someone other than the one using it in connection with sale, for the writer (or the one who employs or who can control the writer) can always determine the content and length of a writing. The term used in the industry to refer to the exempted publications—"third-party literature"—supports reading the term as referring to writings about scientific information produced by those not involved in promotion of products.[166] A statutory change should be considered if the term "publication" in DSHEA cannot be interpreted to be limited to publications authored independently of the sellers of products.

Some further examination of the scope of the exemption is also appropriate in view of the treatment of "off-label" use claims permitted for new drugs under a recent legislative change. That legislation for the first time allows manufacturers of approved new drugs to distribute unabridged information from scientific or medical journals, or reference publications, about clinical investigations considered to be scientifically sound by experts, when the manufacturer files a supplemental application with the FDA that provides for any additional research that may be needed.[167] Ironically, dietary supplement manufacturers appear to have a greater ability to use publications to promote sales to consumers about "off-label" disease use. This is especially surprising because the consumer purchases the supplement directly without consulting a physician for a prescription, as ordinarily occurs with a new drug.

Consideration is needed concerning whether the publication exemption for supplements should have limits similar to those applicable to new drugs, including limiting the scope to the same type of scientific publications, and providing for additional research testing. Supplement manufacturers may believe that they should be able to use publications to make claims with fewer restrictions and fewer testing requirements than those that apply to pharmaceuticals because of the difficulties they have had in patenting natural products and financing drug testing. However, there should be a concern with protecting the consumer interest and equitable treatment. To the extent research incentives are a

166. *See id.* (describing "third-party literature" as "the term often used within the industry" to refer to exempt publications); *compare* BASS & YOUNG, *supra* note 56, at 51 (recognizing that the exemption provision "often is referred to as sanctioning the use of 'third party literature,' but stating there is "no restriction on who may author a 'publication' ").

167. *See* Pub. L. No. 105-115, § 401, 111 Stat. 2296, 2356-61 (1997) (to be codified at 21 U.S.C. §§ 551, 552 & 554). If the publication exemption in DSHEA cannot be interpreted to be limited to scientific publications, a statutory change should be considered.

factor, more study is needed of ways to provide these incentives, as discussed below.[168]

Limits also are needed on the use of publications in connection with the sale of supplements when the publications promote uses, such as treatment for depression, that require a prescription because of the need for medical supervision.[169] Publications also should not be used to promote claims that have been found to be inappropriate dietary claims for use on the label. Thus, publications should not suggest recreational drug uses for ephedra, or make medical claims for "herbal phen-fen" substitutes or other claims that are not permissible dietary label claims. A "publication" promoting such uses may fail to meet the requirement that it not be misleading, but more consideration is needed of the general eligibility of publications to promote these types of non-dietary uses.[170]

### b. Ensuring a "Balanced View"

The Commission also recognized the particular difficulties in ensuring that publications give a "balanced view" of the available scientific information. Scientific articles reporting on research or reviewing the literature generally are well-balanced, but these articles are not likely to be "consumer friendly."[171] In practice, most publications presently used under this provision of DSHEA are specially prepared and are directed to consumers. The Commission report described the balanced view requirement as involving "a need to acknowledge negative as well as positive data and to indicate which

168. *See* discussion *infra* pt. V.B.3. The new law applicable to pharmaceuticals authorizes the FDA to make exemptions from the provisions on additional testing in limited cases in light of factors such as lack of exclusivity and limited size of patient population. *See* § 401, 111 Stat. at 2359-61 (to be codified at 21 U.S.C. § 554). The legislative history indicates this exception is to be limited. Joint Explanatory Statement of the Committee of Conference, 143 CONG. REC. H10475, H10477 (daily ed. Nov. 9, 1997). Similar factors should be considered for supplements for which manufacturers are obliged to do additional testing in connection with new uses promoted in publications.

169. The need to prevent deception may limit the use of publications for prescription drug uses. *See* 21 U.S.C. § 343-2(a)(1). To avoid being misleading, the publication would need to warn consumers not to use the product without medical supervision, but the use by the seller of the publication to promote over-the-counter sale to consumers could be seen as undercutting the warning in a way that is deceptive.

170. If the use is a prescription use, the use of a publication to promote that use can be misleading. *Id.* If the name or potent effects of the product indicate that it is to be used for drug purposes, the exemption would not be applicable since it relates to use "in connection with the sale of a *dietary supplement.*" 21 U.S.C. § 343-2 (emphasis added); *see* discussion *supra* pt. III.B.2.

171. COMMISSION REPORT, *supra* note 16, at xi & 46.

position is supported by the weight of the evidence."[172] The Commission did not develop a set of guidelines on what constituted balance, but it recommended that the FDA undertake "proactive monitoring" and provide regulatory guidance as needed.[173]

Some believe that a particular publication need not be balanced so long as it is displayed with other publications to provide an overall balanced view.[174] DSHEA provides two ways to provide a balanced view: either by display or presentation, or by display or presentation "with such other items on the same subject matter" so as to present a "balanced view."[175] There are "particular difficulties" in trying to provide a balanced view by displaying positive with negative publications, and some Commission members recognized that further study is needed to determine whether there are adequate and reliable means to ensure a balanced view in such a setting.[176]

One difficulty is that the display of material to counter unbalanced material would probably be made at the retail level, but the economic interest of retailers can cut against providing the material on a consistent and reliable basis. If one accepts that a particular publication can be unbalanced, perhaps what is needed is a regulatory requirement that an unbalanced publication prominently state on its cover that it is unbalanced and that consumers need to consult specified other publications to obtain an overall balanced view.

DSHEA precludes false and misleading statements in provisions separate from the balanced view requirement.[177] Congress may have had a special concern with the need for balance as a way to prevent deception because of the difficulty consumers have in evaluating complex scientific information about a product that can affect their health. This interconnection between the means to prevent deception and the need for a balanced view provides support for the congressional ability to impose such a requirement consistent with the Constitution.[178]

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172. *See id.* at 46.

173. *Id.* at xi & 48.

174. *See* BASS & YOUNG, *supra* note 56, at 51-52 (presenting the view that, while a balanced view is necessary, that can be presented within a single publication; however, display with other material is needed when the publication itself is unbalanced).

175. 21 U.S.C. § 343-2(a)(3) (1994).

176. *See* COMMISSION REPORT, *supra* note 16, at 47.

177. *See* 21 U.S.C. § 343-2.

178. The Supreme Court has recognized that the First Amendment does not protect commercial speech that is misleading. *See* Central Hudson Gas & Elec. Co. v. Public Serv. Comm'n, 447 U.S. 557 (1980); *see also* Nutritional Health Alliance v. Shalala, 953 F. Supp. 526 (S.D.N.Y. 1997) (addressing constitutionality of requirement for regulations on health claims).

## E. *Safety of Dietary Supplements*

### 1. DSHEA Exemption from the Food Additive Requirements

DSHEA exempts dietary supplements from being considered food additives.[179] Ordinarily, any substance added to food that is not generally recognized as safe requires approval by the FDA in advance of being sold.[180] In the past, the applicability of the food additive premarket approval requirement was a means of limiting the sale of some supplements, even apart from the restrictions imposed by the drug efficacy requirements.[181]

The food additive provisions made it much easier, in theory, for the FDA to ensure the safety of the supplements. The FDA did not have to prove the lack of safety of an additive—only that the safety was generally unknown to experts. On the other hand, the FDA did not always seek to enforce these food additive requirements rigorously, and acted primarily when specific problems had been identified.[182] When the FDA stated its intent to apply the requirements to amino acids in the FDA Advance Notice,[183] the prospect of the removal of the products from sale helped lead to the enactment of DSHEA.[184]

Court decisions had narrowed the applicability of the food additive provisions to supplements even before the enactment of DSHEA. When a product consists solely of a "single active ingredient" packaged in an inert gelatin capsule, the courts have refused to view the combination as falling within the definition on the basis that there has been no effect on the characteristics of a food, or no addition of a substance to a food.[185]

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The scope of Congress' ability to regulate speech that is truthful in order to promote a public purpose is much debated and beyond the scope of this Article. *See, e.g.*, 44 Liquormart v. Rhode Island, 517 U.S. 484 (1996).

179. *See* 21 U.S.C. § 321(s)(6).

180. *See* 21 U.S.C. § 321(s); 21 U.S.C. § 348 (1994).

181. *See* Stephen H. McNamara, *FDA Regulation of Ingredients in Dietary Supplements After Passage of the Dietary Supplement Health and Education Act of 1994: An Update*, 51 FOOD & DRUG L.J. 313, 315 (1996) (reporting that, before DSHEA, FDA "allegations" of food additive status "had resulted in the end or curtailment of marketing for many products").

182. *See* discussion *supra* pt. II.C.

183. *See supra* note 58.

184. *See* discussion *supra* pt. II.D.; Kassel, *supra* note 48, at 269 (reviewing safety issues and concluding before the enactment of DSHEA that the "present climate of public opinion seems to favor unlimited distribution of dietary supplements, but a supplement-related health disaster could push the public opinion pendulum in a very different direction").

185. *See, e.g.*, United States v. Oakmont Inv. Co., 987 F.2d 33 (1st Cir. 1993); United States v. Viponte Ltd. Black Currant Oil, 984 F.2d 814 (7th Cir. 1993). The latter court noted the relevance of consumer choice: the labeling requirements of the law protected consumers,

### 2. Safety Provisions of DSHEA

In the place of the food additive provisions, DSHEA gives the FDA the authority to bring court actions with respect to supplements sold before the enactment of DSHEA when the product poses a "significant or unreasonable risk" of injury under the conditions recommended or suggested in the labeling.[186] This court enforcement approach is similar to that used at the beginning of the century.[187]

For new ingredients in supplements not in use before 1994, the manufacturer has the burden of affirmatively substantiating the safety of the ingredient based on historical use or scientific information.[188] The manufacturers must notify the FDA of the basis for the information that is the basis for the determination that the product is reasonably expected to be safe.[189]

### 3. Analysis

The substantiation model used by DSHEA for new ingredients provides an intermediate approach between pre-market review and a reactive court enforcement model. There are, however, difficulties with respect to the scope of the substantiation obligation and the adequacy of the FDA's resources and authority to enforce the provisions.

For "grandfathered" pre-1994 supplements, the FDA has the burden to affirmatively prove the existence of a significant or unreasonable risk, a showing that is particularly resource-intensive.[190] Moreover, the absence of a substantiation obligation sends the wrong message to irresponsible manufacturers—namely, that they can sell a questionable product until the FDA "catches" them. Instead, the manufacturer should be affirmatively responsible to ensure that the product is safe.

The substantiation obligation should extend to all supplements, and especially to those that contain a new statement of nutritional support or other new claim, or that recommend any increase in dosage or exposure that can increase safety risks. As long recognized, the safety

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"enabling persons to weigh for themselves the benefits and risks of consuming [Black Currant Oil]." 984 F.2d at 820.

186. *See* 21 U.S.C. § 342(f).

187. *See, e.g.*, United States v. Lexington Mill & Elev. Co., 232 U.S. 399 (1914).

188. *See* 21 U.S.C. § 350b (1994). The statute refers to a specific date, Oct. 15, 1994. For convenience, this Article refers simply to the year.

189. *See* 21 U.S.C. § 350b. The FDA has issued rules to govern the matters to be included in the notification letter. *See Premarket Notification for a New Dietary Ingredient*, 62 Fed. Reg. 49,886 (1997) (to be codified at 21 C.F.R. 190.6).

190. *See* COMMISSION REPORT, *supra* note 16, at 22.

of a product depends upon the dose.[191] Changes in the recommended uses can affect the safety of the product, and such changes need careful evaluation by the manufacturer. When a change is one that experts would view as affecting the safety of the product, the manufacturer should undertake testing or other evaluation that experts would find necessary to ensure that the product is safe. A history of marketing before 1994 does not necessarily provide assurance that the product met the rigors of the food additive provisions, given the judicial narrowing of the FDA's food additive authority and the limited FDA enforcement of the provision.

The FDA can take some steps under the present law to make manufacturers of supplements more responsible for determining the safety of older supplements. The FDA could require supplements whose safety has not been substantiated to bear a warning that the safety has not been determined—a requirement that the FDA has imposed on cosmetics to prevent consumer deception.[192] The warning requirement would not directly require substantiation, but the need for a warning would be a significant inducement to manufacturers to provide it and would prevent consumers from being misled that the product has been tested.[193]

Another approach would examine the scope of DSHEA's grandfather provisions as it applies to increases in the dose above the level the ingredient may have had in the food supply before 1994. DSHEA is a deeply-compromised statute, and on this matter, as on others, its provisions pull in different directions. DSHEA precludes new ingredients without substantiation unless they are ingredients "present in the food supply as an article used for food" in a chemically unaltered form, a test that might seem to require substantiation of old ingredients used at higher levels or new uses that go beyond food uses.[194] On the other hand, DSHEA defines a new ingredient as not including "any dietary ingredient which was marketed" before 1994, a provision indicating that changes in dose levels do not make a supplement "new."[195]

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191. *See Lexington Mill*, 232 U.S. at 411-12.

192. *See* 21 C.F.R. 740.10 (1997). *Cf.* Peeler & Cohn, *supra* note 145, at 354 ("[A]n unsubstantiated claim of safety or a failure to disclose any significant or unreasonable risk . . . could constitute a violation of the FTC Act.").

193. *See* COMMISSION REPORT, *supra* note 16, at 25 (statement of individual member of the Commission).

194. 21 U.S.C. § 350b(a)(1). The FDA's procedures for notification for new ingredients call for information on the level of use. *See Premarket Notification for a New Dietary Ingredient*, 62 Fed. Reg. 49,886 (1997) (to be codified at 21 C.F.R. 190.6).

195. 21 U.S.C. § 350b(c); COMMISSION REPORT, *supra* note 16, at 20 (stating the view that changes in dose do not make a supplement new).

Arguably, one way to reconcile these provisions might be to view the new ingredient category as including any ingredient that is used at levels significantly higher than those in common use in 1994 for either food or dietary supplement purposes. Such a reading would reach changes in the level of use that could affect safety, but not require a notification to the FDA of minor changes that experts would not view as cause for concern. Reading the provision to encompass this type of change in the level of use provides a better assurance of safety, but whether the text permits the reading is open to debate.

The FDA also should identify the type of testing and scientific support needed to substantiate the safety of supplements. Since the safety of supplements is important to health, consideration has to be given to the need for significant scientific agreement to adequately substantiate safety. Ensuring that there is significant scientific support for the safety of supplements needs to be considered for legislative action if the present law does not provide sufficient authority.

Obtaining that level of support involves making the tests available to the scientific community. Manufacturers, however, may resist a requirement that would necessitate making publicly available tests or support developed by them that they regard as confidential business information vulnerable to use by their competitors. An examination is needed concerning whether a process of independent expert review, combined with provision of the full information to the FDA, and a summary for the scientific community, would be viewed as sufficiently reliable indicator of scientific agreement to provide substantiation when clear testing criteria exist to determine safety.

### F. *Resources and Enforcement Model for Regulation*

The FDA's ability to enforce the manufacturer's obligation to meet any substantiation obligation effectively (including the obligation of the manufacturer to substantiate statements of nutritional support) is not clear.[196] The FDA does not have the express authority to inspect the documentary records of food and supplement manufacturers. The FDA has proposed regulations that would require manufacturers to provide access to files needed to determine whether certain requirements relating to nutrient content and health claims on foods have been met.[197] The FDA's authority to impose these types of requirements is debatable and has not been tested. If the FDA does not have that authority under the existing law, Congress should enact legislation to require all supplement

196. *See* discussion *supra* pt. III.C.3.

197. *See* 61 Fed. Reg. at 3885 (1996); COMMISSION REPORT, *supra* note 16, at 26 (statement of individual member of the Commission).

manufacturers to substantiate the safety of their products, and to give the FDA the power to inspect substantiation files.

The adoption of a court enforcement and substantiation model, instead of a pre-market approval model, to determine the safety of supplements has an important impact on the ability to enforce the law. When pre-market approval is required, but the agency does not act promptly on requests for approval, the product is not sold to consumers and delay has an adverse impact on industry applicants. The industry, thus, has a stake in ensuring that the agency has the personnel and resources to meet its statutory review responsibilities. As a result, the drug industry has supported the imposition of user fees for new drug applicants as a way of providing the FDA with more resources, and the FDA has acted faster on applications.[198] When the agency can only take enforcement action in court, the less responsible members of the industry do not have the same concern with being sure that the agency can bring enforcement action when needed.

The Commission recognized the need for the FDA to have adequate resources to enforce the safety requirements of DSHEA in order to protect the public and to maintain public confidence in the safety of the products as a whole.[199] Indeed, the FDA has been urged to act faster to bring enforcement action to deal with the safety problems raised by the sale of ephedra-containing products, such as herbal ecstasy, which have caused deaths and other injuries at high levels.[200] In this era when balancing the budget is a high governmental priority, it can be difficult to obtain additional resources for enforcement measures, however. More study is needed of ways to ensure adequate resources when Congress has adopted an enforcement/substantiation model relating to health regulation.

### G. *Summary*

Overall, DSHEA provides an expanded opportunity for dietary supplements—particularly the non-nutritive ones—to make structure and function claims without being subject to drug regulation. Uncertainties remain, however, about the appropriate scope of these claims and the type of substantiation needed. What limits are ultimately established will affect how readily manufacturers can make claims that indicate, in some indirect way, the usefulness herbal and other supplements may have in

198. *See* 21 U.S.C. § 379h (as amended by § 103, 111 Stat. at 2299-2304) (regarding user fees for prescription drugs)).

199. *See* COMMISSION REPORT, *supra* note 16, at vii & 26.

200. *See id.* at vii & 22. The FDA has proposed rules to limit the use of ephedrine alkaloids in dietary supplements. 62 Fed. Reg. 30,678 (1997); *see* discussion *supra* pt. III.C.2.b.i.

preventing and treating diseases. The publication exemption also creates an opportunity for sellers of supplements to provide scientific information about the uses of supplements for disease purposes. The bounds of this exemption and its limitations are not fully determined.

The FDA needs to provide guidance concerning the appropriate scope of these new provisions, to take steps to limit inappropriate claims, and to test its authority to obtain access to the supporting records when needed. The FDA needs, as well, to consider requiring a warning on supplements marketed before DSHEA that have failed to substantiate their safety. Such a requirement would at least legally oblige manufacturers of all supplements to take affirmative steps to determine the safety of their products, a measure that is especially necessary when dosage levels significantly increase.

## IV. THERAPEUTIC CLAIMS FOR SUPPLEMENTS THAT MEET THE DRUG EFFICACY REQUIREMENTS: THE ROLE OF THE OTC REVIEW

Even with the expansions in DSHEA, dietary supplements cannot be offered with claims on the labeling that clearly relate to use in treating or preventing disease unless they meet the legal requirements for testing and FDA approval or general recognition. Before considering whether there should be an alternative system for disease claims on supplements, it is important to understand the existing legal requirements governing drug claims and to recognize that some supplements may be able to meet the present requirements. These matters are considered below, along with the recommendations of the Commission to facilitate FDA review of OTC drug claims for botanical supplements.

### A. *New Drug Applications*

Any "new drug" needs pre-market approval by the FDA, based on a new drug application (NDA), that shows the product is safe and effective through adequate and well-controlled studies.[201] Obtaining approval of an NDA is a time-consuming and costly endeavor.

In the past, the FDA required that the active ingredients of a new drug be fully identified to determine their contribution to efficacy. Herbal products could not ordinarily meet this requirement because of the complex nature of natural products. The FDA no longer requires this full characterization of natural products so long as adequate compositional data are submitted. Additionally, the FDA has accepted a few investigational new drug applications (IND) for natural prod-

201. *See* 21 U.S.C. § 355.

ucts.[202] Clinical testing is also underway on an expedited basis for claims relating to certain botanical products.[203]

Conceivably, manufacturers of herbal products or other supplements could seek approval of an NDA. New drugs are typically sold as prescription drugs initially. Manufacturers of supplements are likely to prefer the other means the FDA uses to recognize the appropriateness of selling a product as a drug, through OTC review.

### B. *OTC Review for Generally Recognized Drugs*

#### 1. History

Drugs can be marketed without FDA approval of an individual approval of an NDA for a particular drug if the drug is "generally recognized as safe and effective" (GRAS/E).[204] That recognition, by definition, makes the product no longer a "new drug," removing the need for an individual approval of an NDA. To be generally recognized, however, products ordinarily must have the same type of tests needed to obtain approval of an NDA and must have been used for a material time and extent.[205] Thus, qualifying as GRAS/E involves an additional element—that of showing general recognition.

The FDA has recognized a large number of products as being GRAS/E, notably the ingredients in many drugs sold over-the-counter. Many of these products had been sold long before the drug efficacy testing requirements were adopted in 1962. The FDA convened advisory committees that reviewed the testing for the OTC drugs. The panels identified the ingredients and uses for which adequate support and general recognition existed, those that were ineffective, and those for which further testing was needed. In a rulemaking proceeding dealing with the ingredients on a generic basis, the FDA recognized some ingredients and uses as GRAS/E, and some not, taking account of the

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202. *See* Nigel Gericke, *The Regulation and Control of Traditional Herbal Medicines*, Traditional Medicines Programme, University of Cape Town, South Africa, at 16 (1995) (unpublished draft, citing statement of Dr. Robert Temple, Director, FDA Office of Drug Research and Evaluation, at the Office of Alternative Medicine Conference on the Role of Botanical in American Health Care, Dec. 1994) (on file with author).

203. *See, e.g., Pharmaprint's Saw Palmetto-Derived Drug in Phase II for Benign Prostatic Hypertrophy*, THE TAN SHEET, Oct. 6, 1997 (reporting tests for claims for benign prostate hypertrophy and for St. John's wort and depression).

204. 21 U.S.C. § 321(g). There also are certain drugs which have been grandfathered from the new drug requirements, but this grandfather status is narrow and is lost if the claims for the product are changed. *See, e.g.*, USV Pharmaceutical Corp. v. Weinberger, 412 U.S. 655 (1973); United States v. Allan Drug Corp., 357 F.2d 713 (10th Cir.), *cert. denied*, 385 U.S. 899 (1966).

205. *See* Weinberger v. Hynson, Westcott & Duning, 412 U.S. 609, 631-32 (1973).

advisory committees' recommendations.[206] This OTC review, which started in 1972, has completed its major work, although the final rules on some minor ingredients remain to be issued. A few herbs were recognized as effective in the OTC review.[207]

### 2. Botanical Advisory Review Panel

The Commission has recommended that the FDA convene an OTC advisory panel for botanical products to review submissions for herbal products that can show general recognition of safety and efficacy for sale as OTC drugs.[208] The current interest of the public in herbs makes it appropriate for the FDA to give serious renewed consideration to these products. Manufacturers of many herbal products may seek to make claims for uses long recognized as OTC uses by the FDA, such as use as a sleep aid, or for treatment of cold symptoms.

The botanical products considered in such a review should meet the requirements of the existing law. The FDA's regulations for OTC drugs require adequate and well-controlled tests. Traditional use and anecdotal evidence is insufficient.[209] There has, however, been some debate about the rigor with which the criteria were applied in the past.

The FDA regulations recognize that there can be waivers of requirements for controlled testing which are not reasonably applicable or essential to the validity of the study, and where alternative methods of investigation are available.[210] There have been few express waivers, and in one case the condition involved "mechanical action" and professional examination.[211] A Supreme Court decision involving OTC drugs recognized that the FDA may have some measure of discretion in applying the GRAS/E standard.[212] The Court stated that "in some cases general recognition" may be achieved without the kind of testing needed

206. *See generally* 21 C.F.R. 330.10 (procedures for classifying OTC drugs as GRAS/E and not misbranded); 21 C.F.R. pts. 330 to 358 (rules on specific OTC categories); Cutler v. Kennedy, 475 F. Supp. 838 (D.D.C. 1979) (discussing the process and legal standards, and rejection of recognition in the final rules of products needing further testing).

207. *See* COMMISSION REPORT, *supra* note 16, at 54, 55 (for example, elm bark as an oral demulcent).

208. *See id.* at xii & 57.

209. *See* 21 C.F.R. 330.10 (1997). Adequate tests can be of different types: placebo concurrent control, dose-comparison concurrent control, no treatment concurrent control, active treatment concurrent control, and historical control. 21 C.F.R. 314.26 (1997).

210. 21 C.F.R. 330.10(4)(ii).

211. *See* COMMISSION REPORT, *supra* note 16, at 55 (citing *Topical Otic Drug Products for Over-the-Counter Human Use: Tentative Final Monograph*, 47 Fed. Reg. 30,012, 30,013 (1982)).

212. *See* Weinberger v. Bentex Pharmaceuticals, Inc., 412 U.S. 645 (1973).

to obtain approval for an NDA, "[b]ut . . . the reach of scientific inquiry . . . is precisely the same."[213]

The Commission recommended that the type of testing done for existing OTC products for a certain use be considered the benchmark in determining what is acceptable testing for herbal products for the same use.[214] That comparability in the level of testing would ensure a level playing field. The botanical products should not be subject to lower testing standards than those that apply to conventional OTC products for the same use, but correspondingly, they should not be subject to higher standards. If more testing is to be required, the FDA should have to justify the result in terms of how it serves the interest of consumers who would be using the products for the same purposes.

The FDA recently has invited comments on a policy under which it would consider foreign data in the OTC review, but only with a considerable showing that the foreign studies are reliable and applicable to the United States population.[215] Detailed information would be needed on adverse reaction reporting and the extent of marketing, which may be difficult to obtain.[216]

## V. STUDY OF ALTERNATIVE SYSTEM FOR THERAPEUTIC CLAIMS FOR HERBAL REMEDIES: CHOICES ON THE RATIONALE AND IMPLICATIONS

While there is a clear possibility that some herbal products may have sufficient testing and recognition to meet the standards for approval under the OTC review, there will be others that will not have the type of scientific testing that is required. The Commission recommended that there be more study of the alternative systems used overseas, and identified some of the important issues that would have to be addressed in such a study.[217] Any study of an alternative to the existing requirements raises the possibility of a recommendation for a lesser standard of efficacy than that required in the United States. Thus, the study, if undertaken, would deal with a major public policy issue. The discussion below is a reflection on the matters that would need to be considered if a full study were to be undertaken.

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213. *Id.* at 653-54 (citing *Hynson*, 412 U.S. at 631).

214. *See* COMMISSION REPORT, *supra* note 16, at 56.

215. *See Advance Notice of Proposed Rulemaking; Eligibility Criteria for Considering Additional Conditions in the Over-the-Counter Monograph System; Request for Information and Comments*, 61 Fed. Reg. 51,625 (1996).

216. *See id.*

217. *See* COMMISSION REPORT, *supra* note 16, at xi-xii, 52 & 57.

### A. *Traditional Use as a Rationale for an Alternative System*

#### 1. Support for Changing the Standard

##### a. International Harmonization

With the globalization of trade there is increasing interest in the extent to which there should be harmonization in the standards of the industrialized countries governing pharmaceuticals.[218] The establishment of the European Community also has led to a process through which the community members work toward a compatible system of drug regulations for prescription drugs and other products.[219]

The rationale for an alternative model for regulating botanical remedies has an analogy in the efforts at harmonizing the regulation of pharmaceuticals. However, it presents a new factor: the need to consider the relevance of traditional use as part of the criteria for determining efficacy. Only preliminary information is available about the criteria used by other countries and a full understanding of the systems used in regulating herbal remedies in other countries would take a major study.[220]

The limited information available indicates that twelve of eighteen industrialized countries have specific mechanisms allowing therapeutic claims for herbal remedies based on a combination of historical and scientific information.[221] In some countries, clinical evidence is required to support a recommended use, while in others traditional use is sufficient for a limited therapeutic claim. Sometimes, disclaimers may be required.[222] In Germany, herbal medicines can be approved, based on a review by an independent Commission called "Commission E,"

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218. *See* Elizabeth C. Price, *Teaching the Elephant to Dance: Privatizing the FDA Review Process*, 51 FOOD & DRUG L.J. 651, 667-672 (1996); Joseph C. Contrera, Comment, *The Food and Drug Administration and the International Conference on Harmonization: How Harmonious Will International Pharmaceutical Regulations Become?*, 8 ADMIN. L.J. 927 (1995). Recent legislation has encouraged the FDA to proceed with efforts at harmonization when it continues consumer protections consistent with the purposes of American and to "move toward . . . mutual recognition agreements . . . [with the] European Union." 21 U.S.C. § 383(c) (as amended by § 410, 111 Stat. at 2372-73; *see infra* text accompanying notes 236-38.

219. *See* Richard F. Kingham et al., *The New European Medicines Agency*, 49 FOOD & DRUG L.J. 301, 301-03 (1994).

220. For additional commentary, see Edgar R. Cataxinos, Note, *Regulation of Herbal Medications in the United States: Germany Provides a Model for Reform*, 1995 UTAH L. REV. 561; Scott Martin, *Unlabelled "Drugs" as U.S. Health Policy: The Case for Allowing Health Claims on Medicinal Herb Labels; Canada Provides a Model for Reform*, 9 ARIZ. J. INT'L & COMP. L. 545 (1992).

221. *See* COMMISSION REPORT, *supra* note 16, at 52.

222. *Id.* at 52-53.

funded by the government, whose members are nominated by professional societies and pharmaceutical companies.[223] The criteria allow approval for herbal medicines in the absence of controlled clinical trials, based on standard literature and review articles, supplementary experimental studies, or "well documented knowledge on traditional use which is supported by significant experimental studies."[224] Apparently, it is also possible in Germany to sell other traditional herbal products that would not meet the criteria for approval by Commission E. These remedies cannot be sold in pharmacies and must be sold with a disclaimer that limits use to that of a tonic, "to support organ functions," or "as a mildly active drug."[225] Herbal remedies are widely used in Germany and reimbursed by health care plans, and the herbal product, St. John's wort, is reported to be more widely used for depression than prescription drugs such as Prozac.[226]

Other Western European countries have their own disclaimers. In Ireland, for example, herbal remedies must bear the following labeling: "Traditional herbal remedy for short-term treatment of slight discomforts and that should be [sic] not be used for extended periods without the advice of a physician."[227]

### b. Research Costs

The difficulties in financing research on generic natural products can be seen as a reason not to insist on controlled studies. The industry has found that the difficulties in obtaining adequate patent protection discourages research that would benefit competitors as well as the companies that finance the research.[228] The "gold standard" of controlled scientific testing can be seen as too demanding for natural products when they cannot obtain protection for research that the patent system makes possible for drugs synthesized and developed by pharmaceutical companies.

### c. "Better Than" the Present

Allowing direct claims regarding the therapeutic benefits of herbal remedies can be thought better than the indirect ways that therapeutic

223. *See* Gericke, *supra* note 202, at 31.

224. *Id.*

225. *Id.* at 33-34.

226. *Morning Edition* (NPR News broadcast, Oct. 3, 1997) (transcript available by calling 1-888-NPR-NEWS).

227. Gericke, *supra* note 202, at 54.

228. *See* COMMISSION REPORT, *supra* note 16, at 69 (reporting public testimony to the Commission).

uses currently are suggested for these products. According to the Commission report, "many botanicals now are being labeled with statements of nutritional support that suggest only indirectly the type of therapeutic use that is traditional for the product. In such cases, the Commission questions whether the statement of nutritional support is adequate to convey to consumers the intended use of the product."[229] According to the Commission report:

> The scientists on the Commission noted that in some cases, current scientific evidence supports such uses. Most Commissioners concluded that consumers would be better served by clear information regarding such uses than by the limited statements of nutritional support permitted by DSHEA. Current efforts to use statements of nutritional support to suggest such uses without overtly stating them may not provide sufficient information to consumers and may also create a climate of deception that serves neither the industry nor consumers.[230]

As an illustration, the Commission cited statements of nutritional support in regard to the effects of Echinaceae purpureae.[231] The statements of nutritional support on this supplement included the claim that it "[n]utritionally supports healthy immune function."[232] In contrast, the World Health Organization (WHO) draft model monographs for Echinaceae state that it is administered as an "immunostimulant, in supportive therapy for colds and infections of the respiratory and urinary tract," and that it "would ordinarily be administered together with other antibacterial agents, such as antibiotics or sulfa drugs."[233]

### 2. *Difficulties with Changing the Standard*

#### a. The Placebo Effect and the Need for Studies

While the rationale for finding a product effective without clinical testing based on traditional use may have some appeal, the position also presents serious difficulties. For instance, the placebo effect is a reality, and testing against a placebo is the best way to determine whether improvement is due to the drug or, rather, some other factor such as hope for improvement, the self-limiting nature of the underlying

229. *Id.* at 48.
230. *Id.* at 56-57.
231. *See id.* at 50.
232. *Id.*
233. *Id.*

condition, or another drug administered with the remedy.[234] These other factors bear on the effectiveness of herbal remedies as well as on the effectiveness of other products. There surely are some traditional remedies that may "cure" a cold, given enough time. Review by an expert panel can provide some additional measure of reliability. However, the judgment of experts is not fully reliable without adequate testing.[235] Without such testing, the criteria used by experts would rest largely on their judgment. Who the experts are and how they are appointed would become critical factors.[236]

Ineffective drugs do not merely pose an economic cost. The drugs can divert users from more effective therapy, and indirectly cause harm. There also are human costs in lost hopes and time.

### b. The Role of International Models

There has been a long debate about whether the United States drug efficacy standards are inappropriate because they delay domestic use of drugs approved overseas.[237] The increased globalization of trade has led to growing interest in harmonizing United States standards with those of other industrialized counties—particularly the standards of the European Union.[238] Congress has encouraged harmonization with other countries if harmonization "continues consumer protections consistent with the purposes" of the U.S. laws, and also has supported efforts to "move toward the acceptance of mutual recognition agreements" with the European Union.[239] While the harmonization of standards can benefit trade and patients in the form of speedier drug approvals and the

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234. The effects attributed to Echineae in the WHO monograph might, for example, be due to the antibiotics or sulfa drugs used in connection with the botanical. *See id.*

235. *See Hynson*, 412 U.S. at 629-30. The *Hynson* Court interpreted the drug efficacy amendments as requiring that general recognition by experts be based on adequate studies. *See id.* at 631-32.

236. The OTC review uses expert panels and provides for waivers. However, these judgments occur within a framework where controlled testing is the norm. This reduces the risk of having the determination turn on purely subjective assessments. *See* discussion *supra* pt. IV.B.

237. *See* Price, *supra* note 218, at 665 (reviewing information on rate of approvals); Michael J. Malinowski, *Globalization of Biotechnology and the Public Health Challenges Accompanying It*, 60 ALB. L. REV. 119 (1996); Note, *FDA Reform and the European Medicines Evaluation Agency*, 108 HARV. L. REV. 2009 (1995).

238. *See* Merrill, *supra* note 60, at 1863 (observing that FDA officials have been "deeply concerned" about suggestions for international reciprocity that may involve "relinquish[ing] decisional responsibility to bodies that devote many fewer resources and less effort to confirming manufacturer claims that their products are safe and effective, even though such suggestions are less threatening than private third party reviews").

239. 21 U.S.C. § 383(c) (as added by § 410, 111 Stat. at 2373); *see* Merrill, *supra* note 60, at 1862-63.

elimination of duplicative testing, it is also important that the legal standards for drug approval not be lowered inappropriately and unwittingly.[240] To the extent that the international standards for herbal products are equivalent to the American standards, the OTC review provides a forum for examining the support for a particular remedy and providing recognition if the standards are met. Efforts to give mutual recognition to the standards of other countries for botanical remedies raises a fundamental difficulty to the extent that the standards make traditional use sufficient to establish efficacy without adequate scientific testing.

### c. Research Incentives and Equity

The difficulty in developing research incentives for generic products does not justify dispensing with adequate testing for products that claim to be effective. The problem is broader than herbal remedies.[241] Manufacturers of herbal remedies also would receive a substantial competitive advantage over other pharmaceutical manufacturers if they could make drug claims without having to undertake the research and testing that contributes so substantially to the high cost of drugs. Herbal remedies would gain the benefit of an uneven playing field in comparison with proven drugs.

The better course would be to provide research incentives to manufacturers of herbal products who perform testing that protects them against free riders. There are limited non-patent protections under the laws governing drugs for manufacturers of products that obtain drug approvals based on new clinical research.[242] More study should be given to ways to develop research incentives for botanical products if additional measures are needed. Perhaps those who rely on the testing done by others should have to either share the costs or pay royalties. Perhaps there should be some type of exclusivity for such claims. For generic agricultural products, there are "checkoffs" for commodities used to finance research that benefits the industry at large.[243] Government research funding may be appropriate for long-term studies of

240. *See* Gilhooley, *supra* note 92.

241. *See* THE KEYSTONE CENTER, THE KEYSTONE NATIONAL POLICY DIALOGUE ON FOOD, NUTRITION, AND HEALTH, FINAL REPORT 77-84 (1996) (recommending more private and public funding of research on diet and disease, and surveying advantages and disadvantages of exclusivity, royalties and other means of providing incentives).

242. *See* 21 U.S.C. § 355(4)(D) (1997); KEYSTONE REPORT, *supra* note 241, at 82.

243. *See, e.g.*, 7 U.S.C. §§ 4501-4514 (1994); OLAN D. FORKER & RONALD W. WARD, COMMODITY ADVERTISING, THE ECONOMICS AND MEASUREMENT OF GENERIC PROGRAMS (1993).

preventative effects where such studies are especially difficult to perform or to finance.[244]

The problem also arose concerning OTC drugs in need of additional studies to meet the standards of the OTC review. These products were also generic products that were no longer patented. The need to establish general recognition precluded any efforts to maintain exclusivity for the research to support claims.[245] Nonetheless, the very need to support the claims by adequate research provided the drug companies making the OTC products the incentive to do the research during the time the products remained on the market.

Moreover, the OTC uses of herbal products for which manufacturers may be seeking recognition do not necessitate long-term or elaborate studies. Proof that a sleep aid or a laxative works does not require a multi-year study. The lack of research incentives for herbal remedies should stimulate study of the means to provide such incentives, but should not lead to a lower standard for determining that a product is effective.[246]

### B. *The Freedom of Choice Rationale*

#### 1. The Supporting Theory

If there is a justification for an alternative system with a lower standard of efficacy, it would seem to be to allow the consumer the freedom to use a product even when the efficacy of the product has not been adequately proven so long as use is on an informed basis, the product is safe, and there are safeguards against indirect harm. The product would not be presented as being effective like other drugs, but as lacking the testing needed to have the usual assurance of efficacy. If such an alternative system were ever to be established, the product would need to bear a disclaimer to alert the user of this difference. For example, the product should bear prominently the following type of disclaimer: "This product has neither been generally recognized as effective by experts, nor approved by the FDA, based on adequate and well-controlled studies."[247] In addition, the labeling should indicate that

244. *See* COMMISSION REPORT, *supra* note 16, at 69, 70.

245. *See* HUTT & MERRILL, *supra* note 29, at 608.

246. The difficulties in doing long-term studies has led to the adoption of a standard based on significant scientific agreement for health claims on foods under the NLEA. *See* discussion *supra* pts. II.E. & III.A. These tests, which can involve epidemiological studies to determine lifetime effects, present difficulties that are different than the type of testing normally involved in establishing the efficacy of OTC drugs.

247. *See* COMMISSION REPORT, *supra* note 16, at 52-54 (example of disclaimer

the product is not intended for continued use without consulting a physician, and, possibly, that the user should exercise judgment when using a product that does not have the support ordinarily needed for drugs.

The case for this type of approach has been suggested by a former head of the FDA's Center for Drug Evaluation in the context of discussion regarding products like Laetrile, a purported cancer cure made from apricot pits:[248]

> It may not be wise . . . to continue the pretense that substances such as laetrile must either be accepted as therapeutic drugs or be suppressed. The drug regulatory law deals with science, and to risk its essential features in the political arena over relatively innocuous products is to court a serious long-term setback to the rational control of powerful chemicals in our society. We may well be better off to tolerate a few follies in our marketplace. But again the choice is between competing good values—do we want scientific rationality or personal freedom? And if we want the latter, are we willing to pay the price of a few frauds here and there?[249]

In my view, a serious study is necessary to understand the implications of a freedom-of-choice rationale and the regulatory structure of an alternative system that rests on that rationale. Based on that type of study, a more informed judgment might be made about the policy tradeoffs, and whether such a system is better than the indirect means of providing freedom of choice through the availability of dietary supplements. The discussion below examines some of the factors that would need to be considered in such a study.

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recommended by individual Commission member).

248. The FDA's statutory authority to apply the new drug requirements to Laetrile, even when use was sought by a dying patient, was upheld by the Supreme Court in Rutherford v. Hayes, 439 U.S. 1127 (1979). The constitutional right of privacy does not require the availability of a particular therapy to a dying patient. *See* Rutherford v. Hayes, 616 F.2d 455, 457 (10th Cir. 1980).

249. J. Richard Crout, *The Nature of Regulatory Choices*, 33 FOOD DRUG COSM. L.J. 413, 422 (1978).

### 2. Implications and Points for Study Under a Freedom of Choice Rationale for Supplemental Aids

#### a. Consumer Protection

The disclaimer suggested above would provide consumers their principal protection against traditional products that simply do not work, or that do not have the support the consumer expects. The consumer would be informed that the support for the product does not meet the "gold standard" of proof of efficacy. They can then make an informed choice to use a product with only a "bronze" or "copper" level of support.

Study would be needed about how to adequately convey the disclaimer in media advertising. A major impact of allowing any alternative category would be the opportunity for these products to make therapeutic claims on TV and radio. It might be necessary to require an oral disclaimer, rather than merely the print statement typically given for more routine information.

Use of a government-funded independent panel to approve claims for traditional products, as is done in Germany, is problematic as a consumer safeguard. Having pre-market approval to assess the strength and weakness of traditional uses is in conflict with allowing the consumer to make the choice. Furthermore, it would put the FDA in the role of evaluating the strength of traditional use as support for permitting therapeutic use, and thereby take the agency away from the area of its scientific expertise.

To give consumers some protection from fraud, the manufacturers should have to substantiate the truth of any specific claims they make, and should be precluded from making misleading claims about the specific support for products. Thus, if a manufacturer were to claim that palm leaves have been traditionally used in Iceland to cure colds, the FDA would be able to examine the affirmative support the manufacturer purports to have, and take enforcement action based on deception about the specific claim. If the manufacturer claims to have support from specific studies, the manufacturer should disclose other information needed to prevent consumers from being materially misled, such as information about studies that produce different results, or that scientists generally do not accept the result.[250] If it is not possible to make a

250. *See* 21 U.S.C. § 321(n) (1994) (calling for consideration of misleading omissions in determining whether a claim is misleading); Research Labs., Inc. v. United States, 167 F.2d 410, 417-20 (9th Cir. 1948).

specific claim about the support for the product without misleading consumers, the labeling should not refer to the specific support.[251]

To enable the FDA to perform this minimal enforcement role, the FDA would need adequate resources. The equivalent of "user fees" should be required of those who market herbal remedies to assure that the statutory safeguards are observed.[252] The FDA also would need clear authority to obtain access to the substantiation file relied on by the manufacturer.

### b. Safety

The products would also have to be safe, with safety determined based on the adverse effects posed by the product, without any weighing of the risks against the benefits. That type of weighing process used in approving drugs[253] is inappropriate when the benefits have not been adequately proven. Such a test for safety also better protects consumers who will be experimenting with the products to determine if they work for them. The manufacturer would have to substantiate the safety of the product. If the product is not generally recognized as safe, the disclaimer on the label should inform consumers of the lack of recognition.

### c. Scope of Remedies Covered

A special category for traditional herbal remedies, with a lower standard of efficacy for making therapeutic claims, will present a classic example of the slippery slope. Criteria will have to be developed to determine what makes something a traditional use. A decision will have to be made whether the category is limited to herbs and plants, or whether it also includes animal parts, like deer antlers, bear claws, and other parts of the anatomy that have a history of use in some traditional medicines. Vitamins, minerals, amino acids, other dietary supplements, and OTC drugs may seek similar leniency, especially if the products are safe and purport to have some studies or use by doctors to provide some equivalent indication of efficacy. Special treatment for herbal remedies would have to be justified on the grounds that traditional use is an especially reliable indicator of effectiveness that distinguishes these

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251. *See* Peeler & Cohn, *supra* note 145 (discussing difficulty in developing qualified claims about differences of opinion in advertising claims).

252. *See* 21 U.S.C. § 379h (as amended by § 103, 111 Stat. at 2299 (creating authority to assess user fees for prescription drugs).

253. *See Hearings Before a Subcomm. of the House Comm. on Govt. Op.*, 88th Cong., 2d Sess. (1954) (testimony of FDA Commissioner George Larrick), *reprinted in* HUTT & MERRILL, *supra* note 29, at 522.

products from others. That distinction will test one's belief in the adequacy of traditional experience to demonstrate efficacy.

Under the freedom-of-choice model, there would be no reason to limit the claims solely to traditional or herbal remedies. Other products would be eligible so long as they bore the disclaimer, were safe, were substantiated as to any specific claims, and were limited to OTC claims when sold directly to consumers.

An appropriate name for this broader category would be "Supplemental Products." That designation helps to indicate that consumers should consider use in relationship to the availability of tested drugs, and should consult their physician about continued use and when the condition worsens.

### d. Limitation to OTC Uses and Incurable Life-Threatening Conditions

If any alternative category were to be legislatively created for safe products, such products ordinarily should be suitable for self-medication. The OTC limitation protects the consumer from indirect harm. Drugs may need to be issued by prescription because of their toxicity or because of the need for a medical diagnosis to be sure that the user is not suffering from a more serious condition with which the symptoms may be confused.

A limitation of the alternative category solely to OTC claims raises a tension with the freedom-of-choice rationale, however. Laetrile to treat cancer has a claimed use that is not an OTC use. Those who are suffering from cancer or other life-threatening diseases for which there is no known treatment will be the ones who are most interested in using alternative products. While sufferers from AIDS, macular degeneration, or other incurable conditions may be the most eager to try something that provides some hope, that hope is likely to be illusory.[254] Still, allowing patients to pursue their hopes for a cure, even if it is not a promising hope, is the choice they want. Those suffering from serious medical conditions for which there is no effective treatment present more sympathetic cases, but also more difficult cases for allowing freedom-of-choice, than those who are using alternatives for minor conditions.[255]

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254. For discussion expressing concern over the availability of drugs without testing and the inadequacy of disclaimers, see George J. Annas, *Faith (Healing), Hope and Charity at the FDA: The Politics of AIDS Drug Trials*, 34 VILL. L. REV. 771 (1989); George J. Annas, *Questing for Grails: Duplicity, Betrayal and Self-Deception in Postmodern Medical Research*, 12 J. CONTEMP. HEALTH L. & POL'Y 297 (1996).

255. *See* John P. Dillman, Note, *Prescription Drug Approval and Terminal Diseases:*

One way to deal with this tension would be to allow the supplemental remedies offered for uses not suitable for self-medication to be available only by prescription. The products would be subject to the same limits discussed above, but the effectiveness claims for the products would appear only in the professional labeling provided to the physician. The same disclaimers would be made available both to the physician and to the patient. The need to consult a physician would provide assurance that the patient had been advised about the conventional therapies and the value of the claimed remedy before the patient choses to use the alternative.

The manufacturer who promotes drugs for incurable serious medical conditions should provide more information to doctors to enable the physician to advise the user about the alternative. The manufacturer should be required to have the drug evaluated by an independent qualified expert who assesses the adequacy of any testing the manufacturer claims to have. The expert also would identify the additional testing that would be needed to determine efficacy under the usual standards. That information would be available as part of the drug labeling provided to the physician, and would be periodically updated. Under this approach, the FDA would identify a list of expert reviewers whom the manufacturer could use to make the evaluation. Further consideration would be needed regarding whether post-approval studies should be required for these products.

Some investigation would also be necessary concerning the ethical issues faced by a physician in prescribing a drug when the physician knows that the product has not been adequately tested. That investigation may need to consider in more depth the type of information the physician should disclose to the patient in these circumstances.

The FDA has recognized that some drugs are appropriately sold over-the-counter even though they are to be used only after consultation with a physician.[256] That model might possibly be appropriate for some supplemental products already sold directly to consumers to treat conditions that need professional diagnosis and treatment. In such a case, the product still would bear the disclaimer described above and would provide instructions and warnings for the ordinary use of the product. The label would not describe the specific therapeutic use on the

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*Desperate Times Require Desperate Measures*, 44 VAND. L. REV. 925 (1991).

256. *See* 44 Fed. Reg. 16,126 (1979) (addressing treatment of vitamin deficiencies); HUTT & MERRILL, *supra* note 29, at 409. While the FDA permits the therapeutic use to be indicated on the label in these cases, the specific use would not be indicated on the label of the remedies covered by this proposal. Only the identity of the supplement and the need for professional consultation would be on the label.

label, but would instead only identify the active ingredient, along with the statement that product is to be used only after consultation with a physician on its usefulness for other purposes.

If an alternative system were adopted, it would presumably not lead to reimbursement of the supplements by insurance plans. Plans that cover drugs typically do not provide reimbursement for over-the-counter or experimental drugs. If a consumer wishes to use a remedy of unproven efficacy, but has to pay the cost, the consumer may consider the decision with added seriousness.

### e. Non-Applicability to Potent Drugs

The alternative system to be studied should be limited to safe drugs even when use is limited to prescription sale. When a drug poses direct risk of physical harm, the efficacy of the drug should be established to justify the risk, or the drug should be part of a genuine study to determine the efficacy of the product that is part of the new drug approval process.[257]

Any alternative system should not replace the need for approval of an NDA for potent drugs. The FDA has developed procedures to speed up the approval of therapies that offer promise in treating life-threatening and serious health-impairing conditions.[258] Congress also has recently adopted further measures to expedite fast track approval of drugs for life-threatening conditions, and to permit investigational uses in emergencies.[259]

### f. Implications for DSHEA

If an alternative system were to be adopted under any rationale, some consideration would need to be given to its potential implications for

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257. For analysis of the FDA's procedures and possible changes, see, for example, Steven R. Salbu, *Regulation of Drug Treatments for HIV and AIDS: A Contractarian Model of Access*, 11 YALE J. ON REG. 401 (1994); Lois K. Perrin, Note, *The Catch-22 for Persons with AIDS: To Have or Not to Have Easy Access to Experimental Therapies and Early Approval for New Drugs*, 69 S. CAL. L. REV. 105 (1995); Ronald Podraza, *The FDA's Response to AIDS: Paradigm Shift in New Drug Policy?*, 48 FOOD & DRUG L.J. 351 (1993); Marsha N. Cohen, *Getting New Drugs to People with AIDS: A Public Policy Response to Lansdale*, 18 HASTINGS CONST. L.Q. 471 (1991).

258. *See* Nancy K. Plant, *Adequate and Well-Controlled Clinical Trials: Reopening the Black Box*, 1 WIDENER L. SYMPOSIUM J. 267, 293-96 (1996) (surveying measures to speed up approval of drugs used to treat AIDS and some other drugs, and noting debate among some activists about the advantages of the conventional testing process).

259. *See* 21 U.S.C. §§ 351-506 (as added by § 112, 111 Stat. at 2309-10) (addressing accelerated approval of drugs for life-threatening conditions); 21 U.S.C. § 561 (as added by § 402, 111 Stat. at 2365-67 (providing for expanded access to unapproved therapies).

DSHEA. Should the scope of "statements of nutritional support" be revisited because such statements might be used to indirectly suggest therapeutic uses? Should such indirect claims be permitted when Congress has legislatively provided for the means for making therapeutic claims?

Would the exemption provisions from labeling of publications about dietary supplements be appropriate if an alternative system were adopted? The publications now can be used to suggest therapeutic uses that do not have the amount of testing or meet the other conditions necessary to be a permissible claim on the label. If therapeutic claims were to be allowed on the label without full testing under the alternative system, but subject to some statutory safeguards and strong disclaimers, would the publications exemption be a means to circumvent these safeguards?

Are there any implications for products sold as dietary supplements that are widely used by consumers for therapeutic purposes, even though the claims by the manufacturer on the products relate solely to use as dietary supplements?

While these questions need study, the industry is likely to oppose any legislative change establishing an alternative system that might be accompanied by a change in the provisions of DSHEA.[260]

## VI. CONCLUSION

The primary focus for the present should be the appropriate interpretation and implementation of DSHEA. Better guidance is needed on ways to distinguish statements of nutritional support from disease claims. Meaningful identification of what makes a claim a dietary one can help make that distinction. Considering the analogy to food uses, linking the claim to use as a food substitute, distinguishing uses unrelated to the diet, and precluding prescription uses that need professional supervision, are important steps in identifying dietary claims.

The publications exemption is particularly troublesome because it enables product promoters to use materials relating to disease claims in connection with sale without any prior FDA review. The Commission

260. Combined Presentation, American Herbal Products Ass'n, National Nutritional Foods Ass'n, and Utah Natural Products Alliance, Combined Presentation to the Commission on Dietary Supplement Labels, Eighth Meeting (Baltimore, Md. 1997) (stating that there should be no separate regulatory category under DSHEA for herbal remedies and related products); Council for Responsible Nutrition, Statement of John Cordaro to the Commission on Dietary Supplement Labels (Mar. 4, 1997) (opposing "the creation of a new statutory or regulatory category for herbal products that would require an amendment to DSHEA").

Report has identified some factors that are helpful in ensuring that the scientific information is balanced and non-misleading. The publications exemption also should be limited to independent writings about the scientific information not written or developed by the manufacturer or seller of the supplement. The applicability of the exempted material to prescription uses that need medical supervision needs further review.

Manufacturers also need to have an enforceable obligation to substantiate the safety of all supplements. The FDA has to be able to enforce the substantiation requirement effectively and efficiently if that obligation is to have any content. Accordingly, the FDA needs to be able to obtain access to the substantiation records of manufacturers both with respect to safety and structure or function claims.

An enforceable substantiation obligation provides an intermediate model for regulation that does not involve pre-market review, but that also does not rely solely on a reactive approach focused on court enforcement. DSHEA can provide a test of this type of intermediate regulatory model as a way of providing consumer protection for products that are labeled for use as a dietary supplement with dietary claims, but not with disease claims.

If supplements are sold for therapeutic purposes, a greater level of regulatory scrutiny is appropriate. To ensure that the disease claims are valid, controlled testing is needed, along with review by the agency to make sure that the testing requirements have in fact been met. The standards and regulatory review should be the same required for other products that make disease labeling claims.

If botanical products or other supplements are to be legislatively exempted from these requirements, policy makers will have to consider the serious issues involved in creating an alternative system of regulation for therapeutic claims. The approach that seems to most warrant study, in my view, would allow therapeutic claims for safe supplemental products of various types simply on the basis of allowing the consumer to exercise their freedom to choose, on an informed basis, to use a drug that has not been adequately proven to be effective. The consumer would need clear disclaimers on the label and in advertisements that the product neither has adequate testing nor the most reliable support. That approach has some theoretical appeal, but there are difficulties in providing understandable disclaimers to consumers. Clear disclaimers about the lack of adequate studies may discourage many manufacturers from being willing to make claims.

Study also would be needed about the extent to which the products should be limited to over-the-counter uses. Consideration might be given to allowing safe products to be used for conditions requiring medical supervision, but only with a prescription or after consultation with a

physician and without making direct claims to the user. In such cases, the manufacturer would also need to provide an independent assessment of the product for use by the physician.

The manufacturer also should be precluded from making any misleading claims about the specific basis relied upon for the claim. The manufacturer would have to substantiate the specific claims. The FDA would be given the inspection authority and resources from fees paid by manufacturers to enforce the limitations.

Even with the safeguards, some may view this freedom of choice alternative as unacceptable. Disclaimers, no matter how candid, may be insufficient to protect consumers from the confusing claims that new-fangled snake oil salesmen might make. Moreover, there is valid concern that any alternative represents a retreat from the present drug efficacy testing requirements, and that further erosion would occur even for potent drugs.

Others may favor a different alternative system. They may favor a system derived from international models that would allow sale based on traditional use, without requiring controlled studies. Approval of the claim by an expert panel may be required, but not the usual FDA review. The products might bear a label statement that indicates the support the product has (such as that it has been traditionally used in certain countries), but not a disclaimer that indicates the *lack* of testing and expert recognition or FDA review presently needed for drugs in the United States. The latter type of disclaimer may discourage sales, and some may believe it unnecessary. On the other hand, without such a clear disclaimer, this type of alternative approach does not seem to be one that adequately protects consumers.

There are drawbacks to the present system and the indirect way that the availability of dietary supplements provides freedom of choice, under DSHEA, to consumers who choose to use supplements for therapeutic purposes, on their own, or based on exempted publications. The difficulty of identifying an alternative that is better, that is acceptable to the industry, and that adequately protects the public, is likely to leave DSHEA, with its ambiguities and limitations, in place.