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FDA vs. Ephedra: Dietary Supplement Regulation Under DSHEA

Harvard Law School third year writing requirement

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ABSTRACT

The Dietary Supplement Health and Education Act of 1994 (DSHEA) dramatically changed the way dietary supplements are regulated in the United States. DSHEA created a new category of products defined as “dietary supplements,” and altered the way in which these products are regulated in an attempt to promote consumer access to dietary supplements. By weakening the FDA’s regulatory control of dietary supplements, DSHEA made it impossible for the FDA to insure the safety of dietary supplements sold in the United States. DSHEA allows most supplements to enter the market without first being tested for safety, and once on the market, DSHEA makes it very difficult for the FDA to remove potentially dangerous dietary supplements. The FDA’s inability to insure the safety of dietary supplements under DSHEA is exemplified by its failed efforts to place tighter restrictions on the sale of dietary supplements containing ephedra alkaloids (ephedra or ephedrine). Despite mounting evidence that supplements containing ephedra alkaloids may be responsible for serious injury and death, the well-funded and politically-connected ephedra industry has successfully fought off all FDA efforts aimed at imposing tighter regulations on ephedra supplements. Changes to existing law, including pre-market testing, mandatory reporting of adverse events, and accurate content labels are necessary if the FDA is to fulfill its goal of policing consumer safety.

I.

INTRODUCTION

In the past couple of decades Americans have become increasingly health-conscious. In addition to participating in physical exercise and modifying their eating habits, people today routinely rely on dietary supplements to help them achieve their fitness goals.¹ Whether their goals include increased strength and speed for athletic competition, muscle growth, mental wellness or weight loss, there currently exists a dietary supplement on the market that purports to aid users reach the desired end results. Too often, however, dietary supplements contribute to, or cause, serious health problems or even death instead of delivering the promised health benefits.

Although partly attributable to the heightened health-conscious attitude of many Americans, the exponential increase in the use and sales of dietary supplements comes largely as a result of loosened regulatory control over the dietary supplement industry.² The Dietary Supplement Health and Education Act of 1994 (DSHEA)³ weakened the Food and Drug Administration's (FDA) regulatory control over dietary supplements and allowed dietary supplement manufacturers to flood the market with supplements that have no proven benefit to users, and some that evidence has shown to be potentially dangerous.⁴ Efforts by the FDA

¹Pete Hartogs, *Report: Dietary Supplement Warning System Lacking* (Apr. 12, 2001), available at <http://www.cnn.com/2001/HEALTH/diet.fitness/04/12/dietary.supplements/index.html> (stating that 60 percent of Americans take some sort of dietary supplement).

²From 1994 to 2000, after the passage of DSHEA, sales of dietary supplements rose by nearly 80 percent, from \$8.8 billion to \$15.7 billion. Sally Squires, *Making a Claim on Credibility*, WASH. POST, Dec. 4, 2001, at HE01.

³Pub. L. No. 103-417, 108 Stat. 4325 (codified at 21 U.S.C. 321, et. seq. (Supp. 1999)).

⁴E. Randy Eichner, Douglas King, Mark Myhal, Bill Prentice & Tim N. Ziegenfuss, *Roundtable: "Muscle Builder" Supplements*, Gatorade Sports Science Institute, volume 10, number 3 (1999).

to assert more regulatory control over dietary supplements⁵ have been frustrated by the supplement industry's well-financed lobbying campaign, with substantial help from many influential members of Congress, primarily senators Orrin Hatch, Republican of Utah, and Tom Harkin, Democrat of Iowa.⁶ DSHEA has made meaningful regulation of dietary supplements by the FDA nearly impossible, especially given FDA's budget constraints and the economic and political influence of the dietary supplement industry. In essence, DSHEA entrusts the regulation of dietary supplements to the supplement manufacturers themselves, creating a situation in which consumer safety may be jeopardized in the name of corporate profit.

Perhaps the most striking example of the FDA's inability to insure the safety of dietary supplements under DSHEA is in its continuing, and thus far unsuccessful, battle to place more restrictive regulations on supplements containing ephedra alkaloids. Despite mounting anecdotal evidence of ephedra-related injury and death, and recent studies published in the *New England Journal of Medicine* (NEJM) and the *Mayo Clinic Proceedings* concluding that that ephedra alkaloids may pose a serious health risk to some people,⁷ dietary supplements containing ephedra are sold without restriction everywhere from gas stations to health food stores.⁸ This paper examines the possible dangers posed by dietary supplements containing ephedra, the FDA's struggle to regulate these supplements under DSHEA and changes in existing law that may help the FDA more effectively protect the safety of dietary supplement users. Section II provides a brief overview of ephedra and its various uses as a dietary supplement. Section III examines the documented dangers associated with ephedra use. Section IV explains how ephedra, and other dietary supplements, are reg-

⁵Dietary Supplements Containing Ephedra Alkaloids, 62 Fed. Reg. 30678 (proposed June 4, 1997).

⁶Paul Solotaroff, *Killer Bods*, ROLLING STONE, Feb. 14, 2002, at 54.

⁷Christine A. Haller & Neal L. Benowitz, *Adverse Cardiovascular and Central Nervous System Events Associated With Dietary Supplements Containing Ephedra Alkaloids*, 343 N ENGL J MED. 1833, 1837 (2000); David Samenuk, Mark Link, Munther Homoud, et al., *Adverse Cardiovascular Events Temporally Associated With Ma Huang, an Herbal Source of Ephedrine*, 77 MAYO CLIN. PROC 12, 12-16 (Jan. 2002).

⁸Paul Solotaroff, *supra* note 6, at 59.

ulated under DSHEA, and details efforts by the FDA and local governments to place tighter regulatory controls on supplements containing ephedra alkaloids. Finally, Section V offers recommendations for more effective regulation of ephedra and other potentially dangerous dietary supplements. The paper concludes that the FDA is unable, under current law and budgetary restrictions, to adequately insure the safety of dietary supplement consumers, as illustrated by the FDA's battle against ephedra alkaloids. The author recommends the following changes to the existing law: 1) require pre-market testing of dietary supplements; 2) require mandatory reporting of adverse events possibly related to dietary supplements; and 3) require accurate content labels on dietary supplements.

II.

EPHEDRA AS A DIETARY SUPPLEMENT

Ephedra alkaloids are derived from the Chinese herb ephedra, a 5000-year-old Chinese remedy for asthma and flu, and are found in many popular herbal dietary supplements in the United States.⁹Ephedrine is the beneficial chemical component of the ephedra herb and has been used in over-the-counter flu and asthma medications in the United States for years.¹⁰It is chemically similar to the addictive illegal drug methamphetamine, differing by only one atom, and similarly acts to stimulate the nervous and cardiovascular systems.¹¹Ephedrine is simply an isolated form of the chemical compound found in the ephedra herb. Once they enter the bloodstream, ephedrine and herbal ephedra are the same substance having the same physio-

⁹Keith Epstein, *Findings of Fact: A Reality Check on Product Claims*, WASH. POST, May 2, 2000, at Z08.

¹⁰Id. Examples of over-the-counter flu and asthma medications currently sold in the United States include Sudafed and Sinutab, which both contain pseudoephedrine (synthetic ephedrine).

¹¹Id.

logical effects.¹² Ephedra alkaloids are found in an increasing number of dietary supplements, are sold under many different ingredient names¹³ and are contained in variety of colorfully named and marketed products in powder, pill, bar, chewing gum, and drink form.¹⁴ Products containing ephedra alkaloids can be found nearly everywhere, from convenience store check-out lines to herbal health food stores.

The primary uses of ephedra as a dietary supplement are to facilitate weight loss and increase energy. Such goals are shared by a wide variety of supplement users, including elite athletes who desire a boost of energy before training or competition, people attempting to treat obesity, and the average person looking for extra energy to get them through the day.¹⁵ The fact that the beneficial effects of ephedra alkaloids are commonly desirable to many different types of supplement users, combined with its ease of availability and aggressive marketing by manufacturers, has made it overwhelmingly popular in the dietary supplement market. Sales of supplements containing ephedra alkaloids rose to \$1 billion in 2000, up from \$800 million in 1999.¹⁶ Three billion doses of ephedra supplements were sold in 1999 with an estimated 12 million American consumers.¹⁷

¹²Guy Gugliotta, *Woman Wins \$13.3 Million Against Dietary Company*, WASH. POST, Feb. 8, 2001, at A08. The fact that ephedrine and ephedra have the same physiological effects they are in the human bloodstream is to be expected since ephedra is merely an herbal source of ephedrine.

¹³Paula Kurtzweil, *An FDA Guide to Dietary Supplements*, FDA CONSUMER, Sep. – Oct. 1998 (revised Jan. 1999). Ingredient names for ephedra alkaloids include ephedra, ephedrine, ma huang, Chinese ephedra, ephedron, ephedra, methyl ephedrine, Chinese joint-fir, bitter orange, country mallow and Brigham's tea. Benedict Carey, *Risks of Ephedra Usage in Spotlight*, L.A. TIMES, Aug. 27, 2001, at Health Section.

¹⁴Names of dietary supplements that contain ephedra alkaloids include Metabolife 356, Ripped Fuel, Diet Fuel, Stacker 3, Natural TRIM, Hydroxycut, Xenadrine RFA-1, Metab-O-Lite, Metabolift, Up Your Gas, Truckers Luv It, Yellow Jackets, Red Rage, Ultimate Orange and Shape Fast. Benedict Carey, *supra* note 13.

¹⁵Interview with Matthew Howard, northern California construction worker, in Berkeley, Cal. (Mar. 2, 2002) (noting that many co-workers on job sites consume ephedra supplements, often at multiples of the recommended maximum dosage, to wake up in the morning and get them through the day).

¹⁶Sally Squires, *supra* note 2.

¹⁷Benj Vardigan, *Ephedra: One Year Later*, Nov. 7, 2001, available at http://www.buildingbetterhealth.com/topic/ephndf?_requestid=80527.

In addition to its use as a nutritional supplement, ephedra also has been marketed and used as an alternative to the illegal street drug ecstasy.¹⁸ Many ephedra alkaloid products have been promoted and advertised on the internet and in magazines “under a variety of brand names with claims implying that these products mimic the effects of controlled substances,” but are herbal or all-natural.¹⁹ Ephedra-based street drug alternatives came under scrutiny following the March 1996 death of Peter Schlendorf, a 20-year-old State University of New York at Albany student, who consumed twice the recommended dosage of an ephedrine product called Ultimate Xphoria while on spring break in Panama City Beach, Florida.²⁰ Mr. Schlendorf’s death heightened public concern regarding “herbal ecstasy” and alerted the popular media to ephedrine use, particularly by college students, as a substitute for illicit street drugs. In April 1996, the FDA issued a warning, stating that “consumers should not buy or consume ephedrine-containing dietary supplements whose labels portray them as apparent alternatives to illegal street drugs,”²¹ and both Nassau County, New York and the state of Florida placed restrictions on the sale of ephedrine products.²² The FDA announced a stronger stance in opposition to the marketing of ephedrine products as alternatives to illicit drugs in a March 2000 Talk Paper and Guidance for Industry, introducing a new policy that states, in part, “street drug alternatives are unapproved and misbranded drugs that can be subject to regulatory action, including seizure and injunction.”²³ The FDA was able to place greater restrictions on ephedrine products promoted as “legal drugs” only because it decided

¹⁸Peter A. Vignuolo, *The Herbal Street Drug Crisis: An Examination of the Dietary Supplement Health and Education Act of 1994*, 21 SETON HALL LEGIS. J. 200, 200-02 (1997).

¹⁹U.S. Food and Drug Administration, *Guidance for Industry: Street Drug Alternatives* (Mar. 2000), available at <http://www.fda.gov/OHRMS/DOCKETS/98fr/001119gl.pdf>

²⁰Peter A. Vignuolo, supra note 18, at 200; June Weintraub, *Adverse Effects of Botanical and Non-Botanical Ephedrine Products* (1997), available at <http://www.hsph.harvard.edu/Organizations/DDIL/ephedrine.html>.

²¹FDA Talk Paper, *FDA Announces the Availability of New Ephedrine and “Street Drug Alternative” Documents* (Mar. 31, 2000), available at <http://www.cfsan.fda.gov/~lrd/tpephedr.html>.

²²Peter A. Vignuolo, supra note 18, at 228.

²³U.S. Food and Drug Administration, supra note 19 (stating that “FDA considers any product that is promoted as a street drug alternative to be an unapproved new drug and a misbranded drug in violation of sections 505 and 502 of the Federal Food, Drug, and Cosmetic Act. Such violations may result in regulatory action, including seizure and injunction”).

that such products are intended for recreational use to affect psychological states, and therefore do not fall under the definition of dietary supplement as defined in the DSHEA.²⁴

III.

THE DANGERS OF EPHEDRA

A.

Like its chemical relative methamphetamine, ephedra stimulates the nervous and cardiovascular systems, increasing the risk of adverse physical events in the human body including hypertension (high blood pressure), stroke, heart attack and seizure.²⁵ An analysis of the FDA Adverse Event Report (AER)²⁶ database by consumer group Public Citizen²⁷ showed that between January 1993 and February 2000 the FDA received 1,398 reports of adverse events associated with ephedra and ephedra-related products, 81 of which were

²⁴21 U.S.C. 321(ff) (defining the term “dietary supplement”).

²⁵Christine A. Haller & Neal L. Benowitz, *supra* note 7, at 1836; David Samenuk, Mark Link, Munther Homoud, et al., *supra* note 7, at 15 (finding that (1) ma huang use is temporally related to stroke, myocardial infarction, and sudden death; (2) underlying heart or vascular disease is not a prerequisite for ma huang-related adverse events; and (3) the cardiovascular toxic effects associated with ma huang were not limited to massive doses); Public Citizen, *Public Citizen Calls on FDA to Ban Dietary Supplements Containing Ephedra* (Sept. 5, 2001), available at <http://www.citizen.org/pressroom/release.cfm?ID=654>. Other reported symptoms of ephedra use include nervousness, dizziness, tremors, changes in heart rate, headache, stomach trouble and psychosis. Linda Ciampa, *Public Hearings Probe Ephedra Safety* (Aug. 9, 2000), available at <http://www.cnn.com/2000/HEALTH/alternative/08/09/ephedra.controversy/index.html>.

²⁶In 1993 the FDA established its Special Nutritional Event Monitoring System to receive voluntary reports of illnesses and death from dietary supplements. Guy Gugliotta, *FDA Takes Aim at Ephedra*, WASH. POST, Mar. 19, 2000, at A22. The FDA’s AER database includes “voluntary reports from public health agencies, consumers and health professionals of adverse events related to nutritional supplements.” Public Citizen, *supra* note 25.

²⁷Public Citizen is a national, nonprofit consumer advocacy organization founded by Ralph Nader in 1971 to represent consumer interests in Congress. Public Citizen, *supra* note 25.

deaths.²⁸The number of adverse events attributable to ephedra is certainly higher than the FDA's numbers indicate because reporting of AER's is voluntary, even for dietary supplement manufacturers.²⁹ Ephedra manufacturers, distributors and lobbyists, such as the Ephedra Education Council, point to the fact that no scientific study has proved a causal link between ephedra and injury or death, when ephedra-containing supplements are used as directed.³⁰The ephedra industry also criticizes the FDA's data on AER's as flawed and incomplete. Those arguing that ephedra is safe cite two recent studies supporting their position. One study performed by Cantox Health Science International found that consuming ephedra under certain specified conditions results in a low occurrence of adverse reactions.³¹According to the Cantox study, conditions for the safe use of ephedra include:

1.

2.

²⁸Id. "Of the 3,309 adverse events analyzed, 1,398 were associated with ephedra and related substances, or 42 percent. Of those, there were 81 deaths, 32 heart attacks, 62 reports of cardiac arrhythmia, 91 reports of hypertension, 69 strokes and 70 seizures. Ephedra is also associated with sleep disturbance, personality disorders, agitation, headaches, hallucinations, gastrointestinal problems and skin eruptions." Id.

²⁹Rita Rubin, *Consumer Group: FDA Must Ban Ephedra* (Sep. 5, 2001), available at <http://www.usatoday.com/news/healthscience/health/2001-09-06-ephedra-usat.htm>. Trial lawyer Chris Grell took a deposition from a dietary supplement company executive who said the company had received "roughly 3,500 complaints" about its ephedrine product, none of which had been reported to the FDA. Guy Gugliotta, supra note 26. As an example of chronic underreporting, Public Citizen states that "the Texas Department of Health reported approximately 500 adverse events related to ephedra between December 1993 and September 1995." Public Citizen, supra note 25.

³⁰Ephedra Education Council, *Scientific Studies and Reports* (2001), available at <http://www.ephedrafacts.com/studies.html#newengland> (noting that the authors of the NEJM article concede that their study does not prove causation nor does it provide quantitative information with regard to risk, and claiming that "[all] studies and reports have demonstrated that ephedra products are safe and effective in contributing to weight loss when used as directed."

³¹Cantox Health Sciences International, *Safety Assessment and Determination of a Tolerable Upper Limit for Ephedra* (Dec. 19, 2000) available for download at <http://www.crnusa.org/CRNCantoxreportindex.html>.

a.

b.

c.

d.

3.

The Cantox study, however, was funded by an ephedra trade group, the Council for Responsible Nutrition, and thus its findings may be viewed with some skepticism.³³ A joint study by Harvard Medical School and Columbia University, conducted by Dr. Carol Boozer, et al., is also cited to support the relative

³³Id.; Ephedra Education Council, *Scientific Studies and Reports* (2001), available at <http://www.ephedrafacts.com/studies.html#cantox>.

safety of ephedra.³⁴It found that subjects given an ephedra/caffeine combination experienced lowered weight and body fat, and had symptoms similar to subjects given an ephedrine/caffeine combination, including increased heart rate and blood pressure.³⁵These results are merely consistent with the fact that ephedra is an herbal source of ephedrine, and affects the human body in the same manner. Like the Cantox study, the Harvard/Columbia study was funded by an ephedra industry trade group.³⁶

Proponents of tighter ephedra regulation point to an in-depth review of 140 of the FDA's AER's performed by Dr. Christine Haller and Dr. Neal Benowitz of the University of California at San Francisco, and published in the *New England Journal of Medicine* (NEJM).³⁷The study, funded in part by the FDA, concluded that consuming ephedra alkaloids had no demonstrated benefit and that "dietary supplements that contain ephedra alkaloids pose a serious health risk to some users."³⁸As a possible explanation for why other studies have found little risk in consuming moderate amounts of ephedra, the authors suggest that serious adverse events may be due to "individual susceptibility, the additive stimulant effects of caffeine, the variability in the contents of pharmacologically active chemicals in the products, or preexisting medical conditions."³⁹The authors concede that their study "does not prove causation, nor does it provide quantitative information with regard to risk," but they maintain that supplements containing ephedra alkaloids should be considered "unreasonably dangerous," especially for people with unrecognized risk factors such as cardiovascular

³⁴Ephedra Education Council, *Scientific Studies and Reports* (2001), available for download at <http://www.ephedrafacts.com/studies.html#harvard>.

³⁵Id.

³⁶Guy Gugliotta, *Report Disputes Ephedra Dosage*, WASH. POST, Dec. 21, 2000, at A12.

³⁷Christine A. Haller & Neal L. Benowitz, *supra* note 7.

³⁸Id. at 1838.

³⁹Id. at 1837.

disease.⁴⁰They suggest a large-scale case-control study to determine the risks associated with dietary supplements containing ephedra alkaloids.

Another study, recently published in the Mayo Clinic Proceedings, found substantial temporal association with reported adverse events and ingestion of ephedra alkaloids.⁴¹An editorial published in the same issue of the Mayo Clinic Proceedings argues that the study, along with the NEJM study, should not be dismissed due to the lack of an established causal relationship between adverse events and ephedra alkaloids, but instead the findings signal a need for more substantive investigations.⁴²The editorial states that, “[r]andomized placebo-controlled studies are needed to establish the magnitude of risks associated with ephedrine alkaloids and to show definitively whether these dietary supplements constitute a public health menace.”⁴³Completion of a comprehensive large-scale study, like the one suggested in the Mayo Clinic Proceedings, is the only way to provide reliable scientific evidence of the safety of ephedra alkaloids as dietary supplements.

Aside from the dangers of an immediate adverse reaction to an ephedra product, at least one study has suggested that users may become addicted to ephedra alkaloids.⁴⁴Dr. Amanda Gruber, associate chief of substance abuse in the biological psychiatry laboratory of the Harvard-affiliated McLean Hospital, conducted a 1998 study of 36 female athletes, and found that nearly 20 percent of them showed “frank ephedrine

⁴⁰Christine A. Haller & Neal L. Benowitz, *To the Editor*, 344 N ENGL J MED. 1096, 1096-97 (2001) (in response to a letter to the editor of the New England Journal of Medicine that suggested that ephedra was likely neither the cause of, nor a contributing factor to, the adverse events studied by Haller and Benowitz).

⁴¹David Samenuk, Mark Link, Munther Homoud, et al., *supra* note 7, at 15.

⁴²Bruce D. Lindsay, *Are Serious Adverse Cardiovascular Events an Unintended Consequence of the Dietary Supplement Health and Education Act of 1994?*, 77 MAYO CLIN. PROC. 7, 7-9, (January 2002).

⁴³*Id.* at 8.

⁴⁴Benj Vardigan, *Bad Business, Part I: Ephedra Supplements*, Jul. 12, 2000, *available at* <http://www.buildingbetterhealth.com/topic/ephreport1?.requestid=76632> (last updated Aug. 1, 2001).

dependence.”⁴⁵Her finding was based on the subjects “needing increased dosages to achieve the desired effects, experiencing withdrawal symptoms after discontinuing its use, and attempting many times – unsuccessfully – to stop taking ephedra.”⁴⁶A link between ephedra and addiction has not been proved, but questions surrounding such a link may be resolved by conducting a scientific study such as the one previously proposed.

B.

Many dietary supplements containing ephedra also contain one or more additional stimulants, usually caffeine.⁴⁷Caffeine is often listed in its herbal form such as guarana or kola nut on the label of dietary supplements, and thus supplement users may not know that they are ingesting multiple stimulants.⁴⁸As noted in the NEJM study, caffeine is likely to enhance the stimulant effects of ephedra and may put the user at greater risk of an adverse event.⁴⁹The NEJM cites a study on interaction between phenylpropanolamine, also an ephedra alkaloid, and caffeine that found that the two drugs have an additive effect on blood pressure.⁵⁰Combining phenylpropanolamine and caffeine in one product was banned by the FDA in 1983 due to health risks.⁵¹Users of dietary supplements that combine ephedra alkaloids and caffeine may also ingest

⁴⁵Id. at 4.

⁴⁶Id.

⁴⁷Paul Solotaroff, *supra* note 6, at 58. Referred to as “stacks,” combining multiple active ingredients into a single dietary supplement has become popular in the supplement industry. Id.

⁴⁸Benj Vardigan, *supra* note 44, at 1.

⁴⁹Christine A. Haller & Neal L. Benowitz, *supra* note 7, at 1837. “By inhibiting adenosine-mediated dilatation of blood vessels, caffeine constricts blood vessels and may increase blood pressure in persons prone to hypertension. Caffeine also augments the release of catecholamines, an effect that, when combined with that of ephedrine, could lead to increased stimulation of the central nervous system and cardiovascular system.” Id.

⁵⁰Id.

⁵¹Id.

high quantities of caffeine in their daily lives, unknowingly putting themselves at greater risk of an adverse reaction caused by drug interaction. Yet many dietary supplement users remain unaware of the dangers associated with the additive effects of such substances.

Even savvy supplement users who carefully keep track of the amounts of ephedra alkaloids and caffeine they ingest may unintentionally consume a dangerous amount of stimulants if the product labels of the supplements they are taking incorrectly list ingredient amounts. The NEJM article cites a study by Gurley et al. that found that 11 of 20 ephedra supplements tested “either failed to list the alkaloid content on the label or had more than a 20 percent difference between the amount listed on the label and the actual amount.”⁵² Correctly labeling the amount of ephedra alkaloids in dietary supplements is of great importance to the public health and should be strictly regulated and enforced by the FDA.

C.

Ephedra-containing dietary supplements are marketed in a variety of ways, depending upon the characteristics of the target consumer. Ephedra supplements found in natural food stores or targeted to an older consumer base are often marketed as a safe, herbal, all-natural way to lose weight or increase energy levels, and have names such as Natural TRIM, Metabolife or Metab-O-Lite.⁵³ Ephedra supplements aimed at attracting high school kids and young adults are sold in places like gyms or convenience stores and go by names such as Ripped Fuel, Red Rage or Thermo Speed, to indicate their potency and quick results.⁵⁴ Product

⁵²Christine A. Haller & Neal L. Benowitz, *supra* note 7, at 1837.

⁵³Public Citizen, *supra* note 25, at 1; Guy Gugliotta, *Health Concerns Grow Over Herbal Aids*, WASH. POST, Mar. 19, 2000, at A01.

⁵⁴Paul Solotaroff, *supra* note 6, at 58.

packaging is also key in attracting consumers, with supplements commonly sold to young adults packaged in brightly colored bottles or wrapping, with outrageous claims printed on them. Ephedra manufacturers have designed products intended to appeal to nearly every demographic in America. Whether your goal is weight loss, enhanced athletic performance or increased energy, the ephedra industry will try to convince you that ephedra will help accomplish it.

The fact that dietary supplements containing ephedra are legal and readily available contributes to the popularly held perception that the supplements are safe.⁵⁵ Consumers are also lulled into a false sense of security by supplements marketed as “herbal” or “natural,” believing these labels connote safety. There also exists the misconception that the government, or FDA, would not allow a harmful product to remain on the market, especially a widely available product that purports to promote good health.⁵⁶ Misplaced reliance on governmental paternalism and the mistaken belief that “all-natural” products are safe likely contribute to the popularity of dietary supplements containing ephedra. If the FDA cannot succeed in placing tighter restrictions on potentially dangerous products, as in the case of supplements containing ephedra alkaloids, it should at least alert the public to the actual dangers of such products so that consumers can make informed choices without relying on incomplete and erroneous information or a false sense of security.

Ephedra manufacturers have gone to great lengths to promote the safe and natural image of their products and have diligently resisted efforts by the FDA, or others, to warn the public of possible dangers related

⁵⁵Id. at 56.

⁵⁶“Look, all that stuff’s legal. If it was dangerous, they couldn’t put it out there,” stated Alex Zarnas, a high school student and supplement user. Id. “The increased occurrence of adverse events related to ephedrine consumption may be partly blamed on misleading marketing, poor labeling and the pervasive misconception of safety.” June Weintraub, *supra* note 20.

to ephedra use. Some manufacturers have avoided reporting adverse reactions from the use of their products, fought FDA attempts at imposing more stringent regulations on ephedra and brought lawsuits against individuals for publicly claiming that ephedra is potentially dangerous.⁵⁷A deposition taken in 1999 from a company executive of E'ola International, a manufacturer of dietary supplements containing ephedrine, revealed that the company had received "roughly 3,500 complaints" about its ephedrine product, none of which were reported to the FDA.⁵⁸Metabolife International, one of the biggest dietary supplement manufacturers in the nation, recently brought a law suit against a television station, a reporter, and a physician based on a show depicting the possible dangers of Metabolife pills.⁵⁹The founder of Metabolife and president of a supplements industry coalition, Michael Ellis, who was arrested in 1990 for conspiring to manufacture methamphetamine, has been one of the leaders of a successful lobbying campaign that has, thus far, blocked federal regulators who wish to place greater restrictions on ephedra because of safety concerns.⁶⁰The use of creative marketing combined with a powerful lobbying effort have helped the ephedra industry downplay the possible dangers of their products, and have contributed to the billion-dollar industry's rapid growth in recent years.

⁵⁷Rita Rubin, *supra* note 29; Benj Vardigan, *supra* note 44. Some members of the medical profession believe that physicians may be hesitant to publish or publicize adverse events because they fear being sued by ephedra manufacturers. Bruce D. Lindsay, *supra* note 42, at 8.

⁵⁸Guy Gugliotta, *supra* note 53, at A01.

⁵⁹*Metabolife Int'l v. Wornick*, 264 F.3d 832 (9th Cir. 2001).

⁶⁰*Id.*; Sean Elder, *The Skinny on Damage Control* (Oct. 20, 1999), *available at* <http://www.salon.com/media/feature/1999/10/20/media/> (noting that Mr. Ellis eventually pled guilty to a lesser charge).

D.

Many ephedra supplements carry labels stating that the product is not intended for use by anyone under 18 years old, but there is no federal law preventing the sale of ephedra to children. Evidence shows that children are increasingly becoming users of ephedra.⁶¹ Although ephedra manufacturers deny that they market to children, kids often are attracted to ephedra products in fruit punch or gum form with brightly colored packaging and claims that appeal to younger consumers.⁶² Ephedra presents an even greater danger to children than to adults because kids are less likely to use appropriate caution when taking dietary supplements and may intentionally take more than the recommended dosage because they are unaware of any possible negative effects or because they miscalculate the danger of the product.⁶³ Children today also are aware of the “legal high” effects of ephedra, and may be more likely than adults to overdose on ephedra while using it as a substitute for illicit drugs.

IV.

FDA REGULATION OF EPHEDRA UNDER DSHEA

A.

⁶¹Guy Gugliotta, *Diet Supplement Marketers Target Kids*, WASH. POST, June 18, 2000, at A01. Of the 140 adverse events analyzed in the NEJM study, at least 10 were under age 18. Christine A. Haller & Neal L. Benowitz, *supra* note 7, at 1834; Paul Solotaroff, *supra* note 6, at 74 (stating that at the General Nutrition Store visited by the author, children as young as 14 years old were allowed to buy ephedra supplements).

⁶²Paul Solotaroff, *supra* note 6, at 58 (noting label claims such as, “[w]ill hit you like a goddamn knockout punch!”).

⁶³*Id.* at 72. “Seemingly every day, I get a call from another kid who’s been hurt by ephedrine,” said John Tiedt, personal injury lawyer from Los Angeles. *Id.*

The Dietary Supplement Health and Education Act of 1994 amended the Food, Drug and Cosmetic Act, creating a new category of products defined as dietary supplements, a subset of foods, and changed the regulatory authority of the FDA over dietary supplements. Under DSHEA, the definition of “dietary supplement” includes:

- A product (other than tobacco) that is intended to supplement the diet that bears or contains one or more of the following:
 - A product intended for ingestion in pill, capsule, tablet, or liquid form.⁶⁵
 - A product not represented for use as a conventional food or as the sole item of a meal or diet.⁶⁶
 - A product labeled as a “dietary supplement.”⁶⁷
 - Products such as an approved new drug, certified antibiotic, or licensed biologic that was marketed as a dietary supplement.

Two significant changes brought about by the passage of DSHEA have resulted in the FDA’s diminished ability to protect consumers of dietary supplements from harm. First, products falling under the definition of “dietary supplement” are not required to undergo a pre-market approval process.⁶⁹ It is now the sole

⁶⁹Laura W. Khatcheressian, *supra* note 58, at 627.

responsibility of the manufacturer to insure that supplements are safe before placing them on the market. Prior to DSHEA, what are now defined as dietary supplements were regulated by the FDA as either “food additives” or “drugs,” and under either classification the manufacturer was required to prove that the supplement was safe prior to marketing.⁷⁰ DSHEA, however, amended the definition of food additive to explicitly exclude dietary supplements.⁷¹ Dietary supplements avoid regulation as drugs as long as manufacturers do not claim the product prevents, treats, or cures a disease.⁷² Consequently, DSHEA has completely eliminated the FDA’s role in determining whether dietary supplements are safe when they come to market.

Second, DSHEA has dramatically weakened the FDA’s ability to remove a potentially dangerous dietary supplement from the market. In order to remove a supplement from the market the FDA bears the burden of proving that the product is “adulterated.”⁷³ Under DSHEA, a dietary supplement is adulterated if it presents “a significant or unreasonable risk of illness or injury” when used as directed on the label.⁷⁴ By placing the burden of proving dietary supplements “adulterated” on the FDA and requiring no pre-market assurance of safety, DSHEA has effectively entrusted the health and safety of dietary supplement consumers to supplement manufacturers.

⁷⁰Id. at 626; Robert G. Pinco & Todd H. Halpern, *Guidelines for the Promotion of Dietary Supplements: Examining Government Regulation Five Years After Enactment of the Dietary Supplement Health and Education Act of 1994*, 54 FOOD DRUG L.J. 567, 567-586 (1999). FDA can prohibit the marketing of a new dietary ingredient “for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury.” 21 U.S.C. 342(f)(C) (1999). Among other restrictions, “new dietary ingredient” does not apply to ingredients marketed in the United States prior to the passage of DSHEA in October 1994. 21 U.S.C. 350(b)(c) (1999).

⁷¹21 U.S.C. 321(s)(6) (1999); Jennifer J. Spokes, *Confusion in Dietary Supplement Regulation: The Sports Product Irony*, 77 B.U.L. Rev. 181, 191-92 (1997).

⁷²Guy Gugliotta, *FDA Rule Provides Wide Leeway for Diet Claims*, WASH. POST, Jan. 6, 2000, at A2.

⁷³21 U.S.C. 342(f)(1) (1999).

⁷⁴21 U.S.C. 342(f)(1)(A) (1999).

B.

Although stripped of most of its regulatory power over dietary supplements, the FDA has continued to fight, albeit unsuccessfully, for tighter regulation of ephedra. The FDA created a special working group in 1995 to evaluate the potential public health problems associated with dietary supplements containing ephedra. In June 1997, in response to the working group's recommendations and the growing number of AER's originating from ephedra use, the FDA released proposed safety measures for ephedra-containing dietary supplements.⁷⁵The FDA proposed to:

1.

2.

3.

4.

⁷⁵U.S. Food and Drug Administration, *supra* note 5.

5.

If the proposal were adopted it would severely limit the uses of ephedra alkaloids in dietary supplements,⁷⁷ and accordingly, it generated an overwhelmingly negative response from the ephedra industry and the industry's supporters in Congress.⁷⁸ The General Accounting Office (GAO), Congress's investigative branch, reviewed the proposal and issued a report critical of the FDA's scientific basis for the proposal, specifically GAO questioned the FDA's methods of collecting AER's and the reliance on data from AER's as a basis for the proposal.⁷⁹ Based on the GAO's criticism and the backlash from the ephedra industry, in April 2000 the FDA withdrew its proposal, in part.⁸⁰

The failed attempt by the FDA to impose tighter restrictions on the use of ephedra demonstrates its inability

⁷⁷Prohibiting the use of ephedrine or ephedra products for more than seven days "would essentially ban ephedrine weight-loss or bodybuilding supplements, because getting those purported health effects requires weeks of use." Lauran Neergaard, *Ephedrine Crackdown* (June 2, 1997), available at <http://www.hcrc.org/news/ephedrin/html>.

⁷⁸The strongest supporters of the supplement industry in Congress have been Senator Orrin Hatch (R-Utah) and Senator Tom Harkin (D-Iowa). Hatch received more than \$100,000 from the supplement industry in the last election cycle alone and Harkin has received at least \$72,000 since 1994. Paul Solotaroff, *supra* note 6, at 56; Guy Gugliotta, *Dietary Supplement Makers Flex Muscle*, WASH. POST, Dec. 25, 2000, at A01.

⁷⁹Bruce D. Lindsay, *supra* note 42, at 8; U.S. General Accounting Office, *Dietary Supplements: Uncertainties in Analyses Underlying FDA's Proposed Rule on Ephedrine Alkaloids* (July 2, 1999), available at <http://www.gao.gov/archive/1999/h299090.pdf>. Objections included: the FDA failed to establish a causal link between ephedra and the adverse events; some consumers deliberately overdosed themselves; and that some consumers ignored warnings about drug interactions and pre-existing medical conditions. Guy Gugliotta, *supra* note 26, at A22.

⁸⁰FDA withdrew its proposals to limit 1) the ephedrine alkaloid level and 2) duration of use. Dietary Supplements Containing Ephedrine Alkaloids; Withdrawal in Part, 65 Fed. Reg. 17474 (April 3, 2000). Congress claimed that the AER's "were sloppy, incomplete and poorly documented." Guy Gugliotta, *supra* note 26, at A22. In April 2000, FDA continued to push for a restriction against the combination of ephedra and other stimulants, and stricter warning labels to highlight the potential for serious injury or death. It collected 134 new AER's between June 1, 1997 and March 31, 1999. The ephedra industry once again criticized the lack of an established causal connection between the adverse events and ephedra and cited the fact that some adverse events may have resulted from consumers deliberately overdosing or ignoring warnings about drug interaction and pre-existing medical conditions. It has yet to be seen whether FDA will pursue its fight for tighter regulations on ephedra in the near future. Id.; Ori Twersky, *Ephedra Safety Under Official Scrutiny, Again* (Aug. 9, 2000), available at <http://webmd.lycos.com/content/article/1728.60268>.

to protect the public from potentially dangerous dietary supplements under DSHEA. Adverse Event Reports are helpful in alerting the FDA to a public health concern, but it is clear that more compelling evidence, such as a long-term scientific study, is needed to enable the FDA to place tighter restrictions on the sale of a dietary supplement, much less remove a dietary supplement from the market.⁸¹ However, since pre-market safety testing of dietary supplements is not required by DSHEA, the FDA is severely limited in its ability to acquire the scientific evidence that Congress and the ephedra industry claim is needed to fulfill the FDA's burden of proving a supplement unsafe.⁸² Without additional funding, which Congress has refused to grant the FDA, the FDA has been forced to rely on AER's as justification for its proposed restrictions.⁸³ Sufficient funding to perform, or sponsor, scientific testing of dietary supplements, along with mandatory reporting of adverse events associated with supplements are needed for the FDA to effectively regulate dietary supplements under DSHEA.

C.

The FDA's inability to effectively regulate the safety of dietary supplements under DSHEA has prompted

⁸¹Bruce D. Lindsay, *supra* note 42, at 8.

⁸²*Id.* "In essence, industry has positioned itself so that well-designed scientific trials are not required to market dietary supplements containing ephedrine. However, when allegations are made about the safety of the products, those who have a vested interest in marketing the supplements decry the lack of scientific evidence. This argument is reminiscent of tactics used by the tobacco industry years ago." *Id.*

⁸³Paul Solotaroff, *supra* note 6, at 56. "In effect, Congress handed us a huge new job but no new money to do it. We have very few field staff and no budget at all to compile the kind of proof that would stand up in court. What we need is help from the public-health community, scientific evidence that these products are harmful," stated Dr. Christine Lewis Taylor, director of the FDA's Office of Nutritional Products Labeling and Dietary Supplements. *Id.* Senator Tom Harkin, D-Iowa, an ardent supporter of the dietary supplement industry, stated that the FDA "has only itself to blame" because it has not made a sufficient case against ephedra. However, Joseph Levitt, director for the FDA's Center for Food Safety and Applied Nutrition, blamed the shortcomings of the June 1997 proposal on a lack of money from Congress. Levitt noted that Congress has twice refused a \$2.5 million request to improve the FDA's tracking procedures for adverse reactions to supplements. Guy Gugliotta, *supra* note 78; Guy Gugliotta, *Unlikely Allies, Harkin and Hatch Aid Industry*, WASH. POST, Dec. 25, 2000, at A4.

some states and local governments to act to impose tighter restrictions on ephedra supplements. As mentioned in Section II, Florida and New York banned the sale of some ephedra supplements following the overdose and death of Peter Schlendorf during spring break.⁸⁴ A number of other states, including California, Texas, New Jersey, Ohio, and Nebraska have at least attempted to place tighter controls on ephedra supplements.⁸⁵ Congress and the ephedra industry have opposed such attempts by states to more closely regulate ephedra supplements, arguing that additional state restrictions would result in inconsistent regulation.⁸⁶

Many athletic organizations, including the International Olympic Committee (IOC), the National Collegiate Athletic Association (NCAA), and the National Football League (NFL) have banned the use of products containing ephedra alkaloids. In September 2001, the NFL notified its clubs that ephedra was placed on its list of banned substances.⁸⁷ The ban came after the deaths of eleven football players, on both the amateur and

⁸⁴Peter A. Vignuolo, *supra* note 18, at 229.

⁸⁵In California, Governor Grey Davis vetoed a bill in September 2000 that would have required stricter warnings on labels of supplements containing ephedra and a toll-free number on the product label. The veto came seven months after the governor received two \$50,000 campaign contributions from ephedra industry giant Metabolife. Guy Gugliotta, *supra* note 78; Citizens For Health, *California Ephedra Bill Vetoed by Governor* (Oct. 2, 2000), *available at* <http://www.citizens.org/DietarySupplements/PressRelease/CalVeto.html>. A more recent California bill proposing similar restrictions on ephedra, and an age requirement of 18 years old for its purchase, was introduced to the state's Senate Committee on Health and Human Services on March 7, 2002. Senate Bill 1750, *available at* http://info.sen.ca.gov/pub/bill/sen/sb_1...50/sb_1750_bill_20020221_introduced.html.

⁸⁶CBS.com, *Food Fight Over States' Rights* (July 15, 2000) *available at* <http://www.cbsnews.com/stories/2000/07/15/national/printable215616.shtml>. The recent passage of The National Uniformity for Food Act of 2001 raises new questions about states' ability to regulate label requirements and dosage amounts more strictly than federal standards. The Act provides for national, uniform labeling and warning requirements, but would apparently not affect states' ability to impose age requirements for the purchase of ephedra products or restrictions on marketing techniques. The website of the Act's sponsor, Congressman Richard Burr, R-North Carolina, claims that the bill "does not address dietary supplements." H.R. 2649, 107th Cong. (2001) *available at* <http://www.house.gov/burr/RBsbills/food107.htm>.

⁸⁷National Football League press release, *NFL Bans Ephedrine, Other Stimulants* (Sept. 27, 2001), *available at* http://www.nfl.com/news/2001/ephedrine_092701.html. The NFL ban also prohibits players from entering into any endorsement arrangements with ephedra supplement manufacturers or distributors. Before the ban, "ephedrine supplements were endorsed by 2000 NFL MVP Marshall Faulk, Indianapolis Colts running back Edgerrin James and New York Giants receiver Joe Jurevicius." Paul Solotaroff, *supra* note 6, at 58.

professional level, in 2001 during or immediately following football games or practices.⁸⁸ Although no clear link to ephedra has yet been established, at least some of those athletes had consumed dietary supplements containing ephedra shortly before their death, raising concerns about safety.⁸⁹

Perhaps Congress believed that the threat of tort liability would provide a sufficient incentive for ephedra manufacturers to responsibly police their industry and keep dangerous supplements off of the market. Although the threat of lawsuits helped prompt manufacturers to place more extensive warnings on product labels, the deterrent effect of tort liability has so far been insufficient to force the ephedra industry to take substantive precautionary steps that would endanger their profits, such as the steps proposed by the FDA in June 1997. The profitability of ephedra products coupled with the difficulty in proving that such products are the cause of any particular injury or death actually provides incentives for ephedra manufacturers to keep their products on the market. When they are sued, ephedra manufacturers are usually able to avoid litigation and settle cases out of court. Between 1994 and mid-1999, supplement companies settled at least 33 personal injury and wrongful death lawsuits involving ephedra or ephedrine.⁹⁰ The cases usually settle quietly with a confidentiality agreement insuring that settlement amounts and any harmful evidence are kept off of the public record.⁹¹ In February 2001, the first case involving an ephedrine-related injury to go

⁸⁸The rash of sudden deaths prompted Henry Waxman, D-California, to urge the FDA to examine the possible role of ephedra in the deaths. Letter from Henry Waxman, Democratic Congressman, California, to Bernard A. Schwetz, Acting Principal Deputy Commissioner, Food and Drug Administration (Sep. 10, 2001) (on file with the author). Explaining why it imposed the ban on ephedra products, the NFL stated, “These substances [ephedra alkaloid products] present significant health issues for athletes and other engaged in strenuous physical activity.” National Football League press release, *supra* note 87.

⁸⁹Paul Solotaroff, *supra* note 6, at 59. “Devaughn Darling of Florida State and Rashidi Wheeler of Northwestern both . . . collapsed on the practice field after taking ephedrine-laced products.” *Id.*

⁹⁰Guy Gugliotta, *supra* note 12.

⁹¹“There is no public litigation. Lawsuits either get snuffed out real quick, because the [plaintiff] firms don’t have the [financial] legs to stay the course, or they get settled like tobacco litigation – with a confidentiality agreement,” said Los Angeles trial lawyer Ward Benshoof who settled a case against Herbalife International in 1997. Guy Gugliotta, *Ephedra Lawsuits Show Big*

to trial resulted in a jury award of \$13.3 million to an Alaska woman who suffered a stroke after taking a weight-loss supplement containing ephedrine.⁹²The bad publicity of litigation and the cost of settlements has caused insurers to raise ephedra manufacturers' liability rates, and has perhaps contributed to much of the industry voluntarily adopting changes in product labeling aimed at preventing consumers from overdosing.⁹³ Voluntary substantive changes to promote safety, though, have not been a result of the threat of legal liability. The tort system's ability to force effective self-regulation of dietary supplement companies has proved limited and insufficient. Meaningful federal regulation is needed to protect the public health.

V.

CONCLUSION AND RECOMMENDATIONS FOR MORE EFFECTIVE REGULATION OF DIETARY SUPPLEMENTS

Nearly eight years after the passage of DSHEA, a growing body of evidence suggests that the FDA is unable, under current law and budgetary restrictions, to adequately insure the safety of dietary supplement consumers. Instead of striking a reasonable balance between consumer access to dietary supplements and safety, DSHEA compromises the safety of all supplement users. By allowing dietary supplements to enter the market before they are proved safe and by making it very difficult to remove supplements once they have reached the market, DSHEA signals a belief by Congress that consumer access to dietary supplements is

Increase, WASH. POST, July 23, 2000, at A01.

⁹²Guy Gugliotta, *supra* note 12 (finding E'Ola International liable for creating an unsafe product, misrepresenting it as all "natural" when it contained synthetic ephedrine in addition to herbal ephedra, and for being negligent in failing to make changes in the product despite warnings from state and federal authorities that it could cause serious illness, including stroke). *Id.*

⁹³*Id.*

more important than public safety. It is time for Congress to act to correct the dangerous imbalance caused by DSHEA. The following changes to DSHEA would allow the FDA to more effectively protect consumers of dietary supplements:

- 1.

Pre-market testing of supplements that have a questionable history of safety, or new supplements which have no safety record at all, would help insure that supplements on the market are safe. Consumers may not be as well-informed about the potential dangers of dietary supplements as Congress assumed in passing DSHEA. Warnings printed on product labels are a step in the right direction but some consumers ignore such warnings, dismissing them as simply a by-product of our litigious society. Many Americans gauge the danger of a product based on the product's range of availability, how it is advertised and where it is sold. Reliance on governmental paternalism for some degree of protection gives rise to the belief that a dietary supplement that may cause sudden death or injury, and yet is widely available and advertised to promote good health, simply would not be allowed on the market. A pre-market testing process, while expensive and time-consuming, would help prevent dangerous supplements from entering the market without unduly inhibiting consumer access to advantageous supplements.

Pre-market testing of dietary supplements would also aid post-market regulation of dietary supplements. Requiring adequate scientific testing of questionable dietary supplements before they can be sold on the market would provide much needed scientific evidence of the safety and possible dangers of supplements. With a testing system already in place, post-market testing of suspicious supplements would be made much more efficient and practical. A system of scientific supplement safety testing would allow the FDA to make better evaluations of whether to remove a supplement from the market, and help the FDA meet its burden

of proving a potentially dangerous supplement adulterated, if necessary.

2.

Mandatory reporting of adverse events would provide circumstantial evidence of injuries and illnesses stemming from supplement use. Such evidence would alert the FDA to possible health risks and allow for more effective tracking of supplement safety. Decisions regarding post-market testing would also benefit from the information gained by mandatory reporting.

3.

Many dietary supplement labels incorrectly list the amounts of active ingredients in their products, putting even a knowledgeable and careful consumer at risk. The FDA should routinely test dietary supplements to make sure the stated ingredient amounts on the labels correspond to the amounts actually found in the products.

ENDNOTES