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I. INTRODUCTION

The Federal Food, Drug, and Cosmetic Act (FDCA) was enacted to protect consumers from injurious and fraudulent foods and drugs. The FDCA's restrictions on misleading and unsubstantiated promotional claims are central to its goal of preventing injury from dangerous and deceptive products. Last year, the Food and Drug Administration (FDA) issued a notice[1] stating its belief that recent court decisions giving protection to commercial speech under the First Amendment may be in conflict with many of FDA's restrictions on promotion, and even with the FDCA itself. The questions posed at the end of the notice challenge the validity of one of the cornerstones of the FDCA: the requirement that before marketing a new product or a new use of a product intended to treat disease, a manufacturer must demonstrate to FDA that the product is safe and effective for its intended use. Indeed, the notice goes so far as to ask whether the promotional requirements now applicable to dietary supplements might, under the First Amendment, be more appropriate for drugs than the current regulatory scheme. Under a dietary supplement model, neither the safety nor the effectiveness of these products would be subject to government review before marketing.

A restriction on commercial speech satisfies the First Amendment if it directly advances a substantial government interest,[2] is based on evidence of real harm and alleviates the harm to a material degree,[3] and is narrowly tailored to meet the desired ends.[4] As described in detail in this article, the evidence on which the promotional restrictions of the FDCA are based more than satisfies the requirements of the Constitution.

Over the last seventy-five years, Congress has held numerous hearings documenting a long and sometimes shameful legacy of deceptive and dangerous claims made by manufacturers of products intended to improve health. As shown in a wealth of congressional documents, the history of the FDCA demonstrates beyond question that without premarket safety *and* effectiveness requirements, deceptive, unsubstantiated claims about health-related products proliferate, at a tremendous cost in human lives. It demonstrates also that postmarket actions against misleading claims are incapable of protecting consumers from unsafe and ineffective products.

Such evidence provided Congress with a more-than-adequate justification for its conclusion that, in the absence of a requirement that manufacturers demonstrate safety and effectiveness for each promoted use before approval, Americans suffer great harm from the promotion of ineffective and unsafe health-related products.

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[1] 67 Fed. Reg. 34,942 (May 16, 2002).

[2] Central Hudson Gas & Elec. v. Public Serv. Comm'n., 447 U.S. 557 (1980).

[3] Edenfield v. Fane, 507 U.S. 761 (1993).

[4] Board of Trustees v. Fox, 492 U.S. 469, 480 (1989).

There also was abundant evidence to support the conclusion that alternatives, such as disclaimers disclosing the state of the evidence supporting a claim, and postmarket enforcement actions, were inadequate to stop deceptive and dangerous products. The record revealed that when there is no requirement to conduct the tests necessary to establish safety and effectiveness, such tests rarely are conducted. Disclaimers cannot in any way address the grave harm to patients caused by a marketplace in which no one is sure which products work and which do not: many patients are denied effective treatment while others risk serious side effects without any benefit that would justify the risk. Postmarket enforcement actions are cumbersome and time-consuming and leave consumers unprotected from dangerous products for months and even years. This evidence is equally relevant to the regulation of drugs, biological products, medical devices, and foods promoted to treat diseases. Thus, there is more than adequate evidence to sustain the constitutionality of the promotional restrictions currently in place under the FDCA.

II. A HISTORY OF HARM FROM UNSUBSTANTIATED AND DECEPTIVE CLAIMS

FDA has questioned the validity of one of the central protections of the FDCA: the requirement that before marketing a new drug or a new use of a drug, a manufacturer must obtain FDA approval by showing that the drug is safe and effective for its intended use. (Although not stated, the safety and effectiveness requirements for biological products and medical devices are questioned implicitly as well.) The agency has suggested that there is inadequate support for the conclusion that promotion of unapproved drugs or unapproved uses causes sufficient harm to justify its strict regulation. It suggests further that consumers can be adequately protected from dangerous and deceptive products through 1) court actions to stop false or misleading claims, after they have been made; and 2) disclaimers.

The history of the FDCA unfortunately is replete with evidence that the regulatory scheme envisioned by the authors of the notice is inadequate to protect consumers from harm, and it carries a huge cost in human lives. In fact, at different times in history, the FDCA has looked much like the scheme envisioned by the Administration. Before 1938, drugs could be marketed without premarket approval for safety or effectiveness. After many Americans died from inadequately tested drugs, Congress required in 1938 that drugs be approved for safety, but not effectiveness. Manufacturers could promote their products for any use and were trusted to make promotional claims that were truthful and not misleading. If FDA concluded that the claims were false or misleading, the agency was required to undertake an enforcement action to stop the claims. When experience revealed that manufacturers were promoting drugs for uses for which they were ineffective and even dangerous, Congress required in1962 that drugs be approved for safety and effectiveness before marketing.

This history has provided Congress with a revealing study of the behavior of the marketplace when there are no, or limited, premarket approval requirements for drugs and other medical products, and of the public health consequences of this behavior. Congressional oversight of the FDCA has demonstrated beyond question that without premarket safety *and* effectiveness requirements, deceptive and unsubstantiated claims about medical products proliferate, at tremendous cost to the public health. It also has demonstrated amply that promotion of unapproved uses is inherently misleading, and that alternatives such as postmarket enforcement actions cannot protect consumers from the harm caused by false and misleading promotional claims.

It is doubtful that anyone in the Bush Administration intends explicitly to undermine premarket safety requirements for drugs or other medical products regulated by FDA. There are, however, indications that some members of the Administration are interested in weakening or doing away with premarket effectiveness requirements, on First Amendment grounds. This article sets out the evidence that Congress relied on to establish premarket approval for effectiveness—evidence that is more than sufficient to meet the tests set forth by the Supreme Court for restrictions on commercial speech.

The 1906 Pure Food and Drugs Act[5] allowed FDA to take action against false labeling claims made about products, but only if the agency could prove intentional fraud. If the manufacturer showed an honest belief in his product, FDA could take no action. In hearings leading up to the passage of the 1938 Act, Congress heard testimony from FDA that Banbar, a product widely promoted for diabetes, was ineffective, and that many diabetic patients were taking it instead of insulin, the only effective treatment for diabetes. FDA had tracked down many of the patients taking Banbar and learned that a large number had died after abandoning their insulin. FDA brought an enforcement action against the maker of Banbar but lost the case because the agency could not prove deliberate fraud.[6]

In response to cases like this, Congress in 1938 modified the law to permit FDA to bring cases against products promoted with false and misleading claims, regardless of whether the manufacturer committed deliberate fraud. Congress did not require that drugs be shown to be effective in 1938; it took the lesser step of requiring that claims be truthful and not misleading.[7] For the next twenty-four years, the U.S. pharmaceutical marketplace operated under a system similar to that suggested in FDA's notice. Manufacturers could promote their products for any uses as long as their claims were not false or misleading. If FDA believed that claims were false or misleading, it had the burden of demonstrating this to a court, while the product was already on the market.

A. *Evidence From House and Senate Hearings in the 1950s and 1960s*

Beginning in the 1950s and extending into the early 1960s, both the House and Senate held extensive hearings on the drug industry. A large part of these hearings focused on the false and misleading promotion of drugs by the pharmaceutical industry.[8]

The evidence developed from these hearings demonstrated that a regulatory scheme that depended on postmarket enforcement against false and misleading promotion was grossly inadequate to protect Americans from serious harm. The hearings showed that the pharmaceutical marketplace was filled with misleading promotional material on which physicians relied, that there was no reliable source of evidence from which physicians could tell effective drugs from ineffective drugs, and that many Americans were being

[5] Pub. L. No. 59-384, 34 Stat. 768 (1906) (repealed in 1938 by 21 U.S.C. § 392(a)).

[6] *Hearings on H.R. 6906, H.R. 8805, H.R. 8941, and S.5 Before a Subcomm. of the Commission on Interstate and Foreign Commerce* 89 (testimony of Walter Campbell).

[7] Pub. L. No. 75-717, § 502, 52 Stat. 1040 (1938).

[8] *False and Misleading Advertising (Weight Reducing Preparations*), *Hearings Before a Subcomm. of the House Comm. on Gov't Operations*, 85th Cong., 1st Sess. (1957) [hereinafter *Weight Reducing Preparations Hearings*]; *False and Misleading Advertising (Prescription Tranquilizing Drugs), Hearings Before a Subcomm. of the House Comm. on Gov't Operations*, 85th Cong., 2d Sess. (1958) [hereinafter *Prescription Tranquilizing Drugs Hearings*]; ADMINISTERED PRICES, DRUGS, S. REP. NO. 448, 87th Cong., 1st Sess. 171 (1961); *The Drug Industry Antitrust Act of 1962, Hearings Before the Antitrust Subcomm. of the Comm. on the Judiciary*, 87th Cong., 2d Sess (1962) [hereinafter *Drug Industry Antitrust Act Hearings*]; *Drug Industry Act of 1962*, *Hearings Before the House Comm. on Interstate and Foreign Commerce*, 87th Cong., 2d Sess. (1962) [hereinafter *Drug Industry Act of 1962 Hearings*].

subjected unnecessarily to toxic drugs whose benefits had been greatly exaggerated or were nonexistent. Public health experts, government officials, physicians, and experts in drug pharmacology testified that:

- hundreds of new drugs were being introduced each year, many of them minor modifications of existing products or combinations of existing drugs, but promoted as significant breakthroughs;[9]
- drugs were being promoted for indications far beyond any responsible evidence of their effectiveness, and even for indications for which they were known to be ineffective;[10]
- intense promotion of these drugs caused physicians to switch from older, cheaper, and more effective drugs to new, but untested drugs; a considerable period usually elapsed before it became widely known that a highly advertised new drug fell short of its claims;[11]
- when an ineffective drug was prescribed, it often replaced an older but effective drug, subjecting patients to side effects without benefits, and to a lack of effective treatment for serious and even life-threatening conditions;[12]
- drugs with serious side effects, such as potent tranquilizers and antipsychotic drugs, were being promoted widely for minor conditions and for vulnerable populations, including pregnant women;[13]
- physicians were being inundated with promotional material from drug companies that was misleading and unreliable, often in subtle ways;[14]

[9] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 60-62 (statement of Sen. Kefauver, quoting Senate testimony of medical experts); *id*. at 211-12 (testimony of Dr. Martin Cherkasky, Dir. Montefiore Hosp.); S. REP. NO. 448, *supra* note 8, at 170, 175-76, 179-80 (proliferation of fixed combinations of antibiotics clouds diagnosis; encourages inadequate dosing, inadequate treatment, and antibiotic resistance; and exposes patients to unnecessary toxicity); *id*. at 203 (testimony of Dr. Louis Lasagna concerning introduction of new steroids with minor chemical differences from older ones); *id.* at 206-07.

[10] DRUG INDUSTRY ACT OF 1962, S. REP. NO. 1744, 87th Cong., 2d Sess. 37 (1962); *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 85-86 (list prepared by FDA of drugs with questionable indications); *Drug Industry Antitrust Act Hearings, supra* note 8, at 66-68 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health); *id.* at 173 (statement of Abraham Ribicoff, Sec'y of HEW) (drug being widely promoted for heart disease despite American Medical Ass'n (AMA) statement that it lacked evidence of effectiveness); S. REP. NO. 448, *supra* note 8, at 183.

[11] S. REP. NO. 1744, *supra* note 10, at 37; *Prescription Tranquilizing Drugs Hearings, supra* note 8, at 116 (statement of Dr. Ian Stevenson, Chairman, Dep't of Neurology and Psychiatry, Univ. of Va.); S. REP. NO. 448, *supra* note 8, at 202 (testimony of Dr. Russell L. Cecil) (new steroids promoted to replace older ones, without adequate evidence of either effectiveness or side effects).

[12] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 62 (statement of Sen. Kefauver); *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 632 (statement of James B. Carey, Industrial Union Dep't AFL-CIO) (MER/29 widely promoted for lowering cholesterol even after shown to cause cataracts; Decadron widely promoted for arthritis after shown to cause severe mental disturbances and other injuries); *id.* at 213 (testimony of Dr. Cherkasky) (drug for serious staphylococci infection shown to be ineffective after marketing); *id.* at 222, 235 (citing article on Deprol, a tranquilizer promoted for use in depressed patients for whom it had been shown to be ineffective, with serious side effects, including addiction, and risk of suicide); *id.* at 460 (statement of Andrew J. Biemiller, Dir., Dep't of Legislation, AFL-CIO, and former Congressman) ("This is an essential measure to protect the user of medicines against wasting his money and delaying adequate treatment of his illness. Ineffective drugs are worse than useless; they are actually dangerous."); S. REP. NO. 1744, *supra* note 10, at 37 (views of Sens. Kefauver, Carroll, Dodd, Hart, and Long); S. REP. NO. 448, *supra* note 8, at 170; *Hearings on Administered Prices in the Drug Industry Before the Antitrust and Monopoly Subcomm. to the Senate Judiciary Comm*., 86th Cong., pt. 14, at 8139 (testimony of Dr. Louis Lasagna) (newer steroids have more side effects than older ones, including growth suppression in children).

[13] *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 215 (testimony of Dr. Martin Cherkasky) (drug marketed to pregnant women even after it was shown to produce birth defects); *id*. at 504-05 (statement of Miles Robinson, M.D.) (three powerful antipsychotics with severe side effects—Librium, Mellaril, and Thorazine—promoted for minor tension and anxiety and for pregnant women).

[14] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 66-68, 72 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health); *id.* at 113 (statement of Dr. Harold Book, Dir. of

continued

- postmarket enforcement actions against misleading claims were almost always futile because they took "months or even years," while the drugs stayed on the market causing harm (an FTC report showed that actions against misleading advertising completed between 1955 and 1957 took from several months up to nine years; by the time the misleading claim was finally eliminated, the company had switched to a new, often equally misleading, claim);[15]
- "educational" efforts by detailmen, widely used by the pharmaceutical companies to promote products out of sight of regulatory scrutiny, and relied on more heavily by physicians than any other source of drug information, were misleading physicians about the true merits of prescription drugs;[16]
- in the absence of an effectiveness requirement, manufacturers rarely carried out adequate effectiveness tests of their products;[17]
- it was impossible for physicians to ascertain which drugs were effective for their claimed uses because of the large number of drugs being introduced, misleading advertising, the absence of adequate effectiveness testing, the fact that the evidence, if there was any, was either unpublished or scattered through hundreds of medical journals, and the lack of time and training most physicians have to devote to the study of detailed clinical reports;[18]
- there was no reliable source of information to which physicians could turn when trying to assess the effectiveness of a drug;[19] and

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Labs., Norristown State Hosp., and Ass't Prof. of Neuropathology, Grad. School of Med., Univ. of Pa.); *Prescription Tranquilizing Drugs Hearings*, *supra* note 8, at 117 (statement of Dr. Ian Stevenson, Chairman, Dep't of Neurology and Psychiatry, Univ. of Va.) (study of drug advertisements showed consistent but subtle deceptions: inflating the quality of cited data, exclusive reliance on unpublished data, use of findings taken out of context, failure to report negative data, emotional appeals through use of images); S. REP. NO. 448, *supra* note 8, at 165-87 (studies of drug ads showed variety of misleading techniques, including use of testimonials, understatement or omission of unfavorable evidence, use of false associations and irrelevant facts, and publication of studies written by drug companies under the name of an independent physician).

[15] *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 63 (statement of Abraham Ribicoff, Sec'y of HEW); *id*. at 463-64 (statement of Andrew J. Biemiller, Dir., Dep't of Legislation, AFL-CIO, and former Congressman) (Federal Trade Commission's (FTC's) attempts to correct false advertising of Doan's pills took several years); *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 171 (statement of Abraham Ribicoff, Sec'y of HEW); *id.* at 66-68, 71 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health); *id.* at 102-03 (statement of Dr. Harold Book, Dir. of Labs., Norristown State Hosp., and Ass't Professor of Neuropathology, Grad. School of Med., Univ. of Pa.); *Weight Reducing Preparations Hearings*, *supra* note 8, at 42 (statement of Maye Russ, Nat'l Better Business Bureau); *id.* at 197-212 (FTC table showing lengthy period of time between initiation of investigation of deceptive claims and final cease and desist orders).

[16] *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 211-12 (testimony of Dr. Martin Cherkasky); *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 80 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health, citing AMA opinion survey of physicians); S. REP. NO. 448, *supra* note 8, at 190-98 (drug company promoted chloramphenicol through detailmen for broad uses despite risk of aplastic anemia, misrepresenting official FDA/NRC warnings).

[17] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 105-06 (statement of Dr. Harold Book, Dir. of Labs., Norristown State Hosp., and Ass't Professor of Neuropathology, Grad. School of Med., Univ. of Pa.); S. REP. NO. 448, *supra* note 8, at 203 (quoting Dr. Louis Lasagna, "adequately controlled comparisons of these drugs are almost impossible to find"); *id.* at 187 (quoting Dr. Dowling, "a number of drugs have been put on the market with efficacy claims based on extremely meager and unobjective observations"); *id.* at 176-77 (quoting Dr. Frederick Meyers, "Much of what passes as clinical investigation . . . is really an effort to get the drug used in a medical center before general release, to get a physician of some influence to use the drug as part of a clinical trial . . . .").

[18] S. REP. NO. 1744, pt. 1, *supra* note 10, at 37; S. REP. NO. 448, *supra* note 8, at 171; *id.* at 204 ("as was repeatedly emphasized during the hearings, detailed clinical reports tend to be perused carefully only by the specialists in the field"); 108 CONG. REC. 19,925-26 (1962); *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 222-23 (testimony of Dr. Martin Cherkasky); *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 76 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health).

[19] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 73 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health); *id*. at 173 (statement of Abraham Ribicoff, Sec'y of HEW, quoting from *JAMA* article by Dr. Isaac Starr); S. REP. NO. 448, *supra* note 8, at 187.

- huge expenditures for the promotion and development of minor modifications of existing drugs left little room for the development of new drugs for significant health problems.[20]

A review by the National Academy of Sciences of drugs on the market before 1962 confirmed that Congress's concerns about widespread promotion of ineffective drugs were more than justified. Over eighty percent of the uses for which drugs were promoted before 1962 were found to lack adequate evidence to demonstrate effectiveness. By the time FDA completed its formal review of pre-1962 drug claims under the Drug Efficacy Implementation Study (DESI), the agency had found that one-third of all drugs (1,099 of 3,443) on the market in 1962 could not be shown to be effective for a single indication and had to be taken off the market. These included widely promoted drugs that were among the top 200 in sales.[21] A large percentage of the remaining drugs also lost one or more of the secondary indications for which they previously had been marketed.

B. *Specific Examples of Harm*

The hearings leading up to the enactment of an effectiveness requirement identified several specific types of harm to which Americans were being subjected to daily from this tide of ineffective and over-promoted drugs. One was the promotion of toxic drugs for uses for which the drugs' benefits did not outweigh their risks. For example, the antibiotic chloramphenicol (Chloromycetin) was promoted for a wide range of uses, from life-threatening to minor infections. When cases of aplastic anemia, a serious and sometimes fatal blood disorder, were shown to be caused by chloramphenicol, FDA required the company to include warnings in the drug's label and both FDA and the American Medical Association (AMA) recommended that the drug's uses be restricted. These warnings about serious and even fatal adverse reactions failed to slow demand, however. Documents provided in congressional hearings showed that detailmen continued to promote the drug as effective for a wide range of uses, resulting in widespread use of the drug for minor infections, and an unnecessary toll of serious adverse reactions and deaths.[22]

Congress heard testimony that drug companies promoted tranquilizers for every type of psychological distress from serious depression to mild anxiety, and added them to a variety of other drugs, from heart disease medications to gastrointestinal drugs.[23] Even mild tranquilizers can be addictive, while many others cause serious, often irreversible side effects. Tranquilizers were later shown to be ineffective in all of the combination products, and unsafe or ineffective for most of the remaining uses for which they were promoted. Thus, consumers were subjected to serious injuries that outweighed any possible benefit.

Some of the widely promoted tranquilizers were, in fact, powerful antipsychotic drugs with side effects so severe that they are now used only for the treatment of serious mental illnesses (i.e., schizophrenia, manic-depression). An advertisement for Thorazine, now reserved for schizophrenia, in the *Maryland State Medical Journal* for July 1962 showed

[20] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 60-62 (statement of Sen. Kefauver, quoting Senate testimony of Dr. Henry Dowling:

Under the present system, a successful pharmaceutical company works at a frenetic pace to produce slight modifications of existing drugs to keep abreast of its competitors . . . the money spent on discovering, developing, and promoting these drugs is largely wasted. This money could be better spent in looking for truly new drugs.);

S. REP. NO. 1744, *supra* note 10, at 48.

[21] FDA Talk Paper, DESI Drug Review for Effectiveness is Concluding (Sept. 17, 1984).

[22] S. REP. NO. 448, *supra* note 8, at 192-98.

[23] *Prescription Tranquilizing Drugs Hearings, supra* note 8.

a beautiful picture of a happy family, with the caption, "Emotional control regained *** a family restored *** thanks to a doctor and Thorazine *** Experience in over 14 million Americans *** A fundamental drug in both office and hospital practice."[24]

Thorazine already was known to cause agranulocytosis, a depletion of white blood cells that is frequently fatal. One expert testified that he personally had seen eleven cases of agranulocytosis and four deaths result from inappropriate prescriptions of Thorazine.[25]

Mellaril, now a drug of last resort for schizophrenia because of its severe side effects—including sudden death—was widely promoted to general practitioners for pregnant women with emotional symptoms in connection with childbirth, and "tense, nervous patients seen in everyday practice *** for chronic fatigue, insomnia, anxiety, and apprehension, vague digestive disorders, etc."[26] An expert testified that he was "impressed with that 'etc.' It just tapers off into the wide, blue yonder where tranquilizers are claimed to be good for everything."[27] Librium, a drug now reserved for manic-depression, was advertised for the "surgical patient who sees doom in the frown of a nurse."[28]

Both Thorazine and Mellaril also cause tardive dyskinesia, a serious and sometimes irreversible movement disorder, in which the patient suffers from involuntary and disfiguring movements of the face, tongue, and body. The severe risks associated with these drugs could never justify their use for such minor conditions as everyday tension or insomnia, and yet that is exactly what they were promoted for in a setting where there was no effectiveness requirement for each promoted use.

These examples illustrate the public health damage that results from a system that approves medical products for safety but not effectiveness, or that permits promotional claims about uses for which the product has not been demonstrated to be effective. Because drugs potentially have serious risks, a drug can be considered safe only when its risks are outweighed by its benefits for particular uses. A drug with significant side effects may be considered safe if it is known to be effective in the treatment of a serious condition, but may be unacceptably harmful for a minor condition, or even for another serious condition, when the drug's benefits for that condition have not been established. Because safety and effectiveness are related inextricably, it is meaningless to say that a drug is "safe" except in relation to a specific demonstrated benefit. Almost no drug can be considered safe for uses for which it has no demonstrated benefits.[29]

There also were examples of ineffective drugs promoted for serious conditions, where other treatments were available. Deprol, a tranquilizer was promoted to general practitioners for all types of depression, including serious depression. A psychiatric expert testified that there was no evidence that Deprol was effective for depression, and that the vigorous promotion of Deprol caused him deep concern about the fate of depressed patients seen by general practitioners.[30] The Secretary of Health, Education, and Welfare testified about the widespread promotion of Clarin for heart disease, despite an AMA determination that the drug lacked effectiveness.[31]

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[24] *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 505 (statement of Miles Robinson, M.D.).

[25] *Drug Industry Antitrust Act Hearings, supra* note 8, at 105 (statement of Dr. Harold Book, Dir. of Labs., Norristown State Hosp., and Ass't Professor of Neuropathology, Grad. School of Med., Univ. of Pa.).

[26] *Drug Industry Act of 1962 Hearings, supra* note 8, at 505 (statement of Miles Robinson, M.D.).

[27] *Id.*

[28] *Id.* at 504.

[29] S. REP. NO. 448, *supra* note 8, at 189-90 (testimony of Dr. Barbara Moulton).

[30] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 62 (statement of Dr. Freyhan).

[31] *Id.* at 173 (statement of Abraham Ribicoff, Sec'y of HEW).

A final example illustrates the grave harm that can befall patients when drug indications do not have to be shown to be effective before they are promoted. In the 1940s and 1950s, diethylstilbestrol (DES) was marketed widely to prevent threatened spontaneous abortion (miscarriage). Because DES was considered safe and effective, it also was promoted and prescribed for normal pregnancies. It has been estimated that between five and ten million American women received DES before FDA issued a warning against its use in pregnant women in 1971.[32] In 1970, evidence began to accumulate that exposure to DES *in utero* caused a high rate of reproductive abnormalities in the daughters and sons of women given DES, including hundreds of cases in girls and young women of a rare form of vaginal cancer previously found only in elderly women.[33] Furthermore, daughters of women who took DES have an increased rate of premature births, casting the shadow of DES toxicity over the next generation.[34] Perhaps the greatest tragedy of DES is that years after it was first marketed, an independent study showed that it was completely ineffective for preventing miscarriages.[35] Even after this study was published, the drug continued to be promoted and prescribed for pregnant women.[36]

Had there been an effectiveness requirement in place when DES was introduced, thousands of men and women would have been spared the serious, sometimes fatal injuries caused by the drug, even though the side effects of the drug were not known at the time the drug was prescribed. But that is the nature of drugs—their true toxicity often is not known until thousands or millions of people have been exposed. Knowing this to be true, it is unconscionable to expose patients to drugs without a well-established benefit for each promoted use.

C. *Unsubstantiated Promotional Claims Shown to Be Inherently Misleading*

The evidence accumulated by Congress before the passage of the 1962 Drug Amendments to the FDCA demonstrated that, without the benefit of premarket review of a drug's effectiveness by an objective body, it simply was not possible for most physicians to discern which products were effective and which were not. Three features of the pre-1962 scheme caused promotional claims about unproven uses to be considered inherently misleading: 1) physicians heavily relied on promotional information from manufacturers, much of which was misleading; 2) existing reliable, objective evidence was difficult or impossible for average physicians to find because they were too busy to track down scattered, often unpublished data on hundreds of new drugs; and 3) in the absence of required testing, few, if any, companies conducted the kind of studies that would provide reliable evidence of their products' effectiveness.[37] In this setting, only

[32] R.M. Guiusti, K. Iwamoto & E.E. Hatch, *Diethylstilbestrol Revisited: A Review of the Long-term Health Effects*, 122 ANN. INTERN. MED. 778-88 (1995).

[33] *Id.*; E.E. Hatch, J.R. Palmer, L.Titus-Ernstoff, K.L. Noller et al., *Cancer Risk in Women Exposed to Diethylstilbestrol* In Utero, 280 JAMA 630-34 (1998).

[34] NATIONAL CANCER INST., NIH, DES RESEARCH UPDATE 1999: CURRENT KNOWLEDGE, FUTURE DIRECTIONS, MEETING SUMMARY (July 19-20, 1999).

[35] W.J. Dieckmann, M.E. Davis, L.M. Rynkiwwicz & R.E. Pottinger, *Does the Administration of Diethylstilbestrol During Pregnancy Have Therapeutic Value*?, 66 AM. J. OBSTET. GYNECOL. 1062-81 (1953).

[36] DES RESEARCH UPDATE 1999, *supra* note 34; D. Ibaretta & S. Swan, *The DES Story: Long-Term Consequences of Prenatal Exposure*, *in* LATE LESSONS FROM EARLY WARNINGS: THE PRECAUTIONARY PRINCIPLE 1896-2000 (P. Harremoes et al., eds., 2000); http://www.desaction.org.

[37] S. REP. NO. 1744, pt. 1, *supra* note 10, at 37, 39 (views of Sens. Kefauver, Carroll, Dodd, Hart, and Long); S. REP. NO. 448, *supra* note 8, at 171; 108 CONG. REC. 19,925-26; *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 222-23 (testimony of Dr. Martin Cherkasky); *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 76 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health); *Prescription Tranquilizing Drugs Hearings*, *supra* note 8, at 123-24 (statement of Dr. Ian Stevenson, Chairman, Dep't of Neurology and Psychiatry, Univ. of Va.) (physicians could not assess the effectiveness of a drug based on their own clinical practices or historical use).

academic specialists had the knowledge and time to ferret out the truth about drug products within their specialties.[38] Even then, there were few, if any, definitive studies on the effectiveness of marketed drugs, leaving even the experts to guess which drugs were effective and which were not.[39]

In the world envisioned by FDA's notice, physicians are able to make rational prescribing decisions primarily based on promotional material from manufacturers and in the absence of access to well-designed, objective studies of effectiveness. As the Secretary of the Department of Health Education and Welfare (HEW) testified in 1962, however, it is meaningless to say that a physician should have the right to decide for himself whether a drug is effective, unless "truthful and complete information" about the effectiveness of a drug is available to any physician in the ordinary course of practice.[40] The marketplace as it existed before there was an effectiveness requirement provided neither. For most physicians, "truthful" information was impossible to separate from misleading information, and "complete information" almost was never available.

Truthful information was impossible to separate from misleading information because promotional material cited scientific evidence in ways that made harried physicians believe they had adequate information to make prescribing decisions. One expert testified about the "exceedingly subtle" methods employed in promotional material to convey the impression that claims were supported by scientific evidence, when, in fact, there was no little or no support for the claims. He provided a representative advertisement that cited seven references to demonstrate the scientific support for the advertised claims. When the expert took the time to look into these references, not one could be shown to support the claims in the advertisement. The first and third cited studies were "in press" and unavailable for review, the second study was uncontrolled and its results had been distorted in the advertisement, the fourth study clearly was misrepresented, and the fifth, sixth, and seventh references were "personal communications" with the company and unavailable for review.[41]

The expert also presented data on a larger review of prescription drug advertising that showed the problems seen in his example were commonplace. In addition, he found that 1) negative studies (studies that failed to show that the drug worked) were never reported in promotional material; 2) data were presented as if they were of high scientific quality when in fact they were not; 3) studies cited frequently were from low quality or foreign publications; and 4) statements and findings in studies were taken out of context.[42] Many other experts testified that promotional material appeared to provide scientific support that was in fact lacking, but in ways that would be difficult for the average physician to detect.[43] Hearings on advertising of over-the-counter drugs showed that promotion to consumers was at least as misleading as that to physicians.[44]

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[38] S. REP. NO. 448, *supra* note 8, at 204 ("as was repeatedly emphasized during the hearings, detailed clinical reports tend to be perused carefully only by the specialists in the field").

[39] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 105-06 (statement of Dr. Harold Book, Dir. of Labs., Norristown State Hosp., and Ass't Prof. of Neuropathology, Grad. School of Med., Univ. of Pa.); S. REP. NO. 448, *supra* note 8, at 203 (quoting Dr. Louis Lasagna); *id.* at 187 (quoting Dr. Dowling).

[40] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 173 (statement of Abraham Ribicoff, Sec'y of HEW).

[41] *Prescription Tranquilizing Drugs Hearings*, *supra* note 8, at 117 (statement of Dr. Ian Stevenson, Chairman, Dep't of Neurology and Psychiatry, Univ. of Va.).

[42] *Id.*

[43] S. REP. NO. 448, *supra* note 8, at 165-87 (studies of drug advertisements showed a variety of misleading techniques, including use of testimonials, understatement or omission of unfavorable evidence, use of false associations and irrelevant facts, and publication of studies written by drug companies under the name of an independent physician).

[44] *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 461 (statement of Andrew J. Biemiller, Dir., Dep't of Legislation, AFL-CIO, and former Congressman); *Prescription Tranquilizing Drugs Hearings*, *supra* note 8, at 37-41 (statement of Maye Russ, Nat'l Better Business Bureau).

"Complete" information almost always was unavailable to physicians, because it did not exist. In the absence of an effectiveness requirement, manufacturers rarely carried out adequate effectiveness tests of their products.[45] Even if it had existed, there was extensive testimony that ordinary physicians lacked the time and expertise to find and distinguish reliable information from the deluge of promotional material.[46]

Where the evidence showed that physicians and consumers had no access to objective information about the effectiveness of drugs, and neither the time nor the knowledge to pin down the truthfulness of promotional material, it was entirely appropriate for Congress to consider such material inherently misleading.

It has been suggested that First Amendment case law precludes restricting a category of commercial speech based on a congressional finding that the speech in question is inherently misleading. In fact, the Supreme Court repeatedly has suggested that unverifiable claims may be banned as inherently misleading.[47] There was no suggestion in these, or later Supreme Court cases, that the misleading nature of unverifiable claims had to be addressed through a disclaimer rather than a ban.

Many also unquestioningly assert that dissemination of "peer-reviewed" journal articles and textbooks by pharmaceutical companies cannot mislead physicians, presumably because these sources are thought to provide the unbiased "truth" about a product. These arguments rarely acknowledge several problems with industry dissemination of peer-reviewed articles that cause them to be misleading. First, there is no guarantee that the disseminated material accurately or fairly reflects the state of knowledge about the use in question. Manufacturers have little incentive to disseminate information that discredits the use of their drug, no matter how relevant and reliable that information is.

The likelihood that dissemination of peer-reviewed articles will result in a misleadingly positive view of a drug is compounded by three problems with reported studies: 1) negative studies are much less likely to be published in general (publication bias);[48] 2) industry-sponsored, peer-reviewed studies are significantly more likely to favor the sponsor's product, either because the industry suppresses negative studies or because industry-sponsored studies are designed to maximize the positive attributes of the product (e.g., by comparing it to another product at a less than optimal dose);[49] and 3)

[45] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 105-06 (statement of Dr. Harold Book, Dir. of Labs., Norristown State Hosp., and Ass't Prof. of Neuropathology, Grad. School of Med., Univ. of Pa.); S. REP. NO. 448, *supra* note 8, at 203 (quoting Dr. Louis Lasagna, "Adequately controlled comparisons of these drugs are almost impossible to find."); *id.* at 187 (quoting Dr. Dowling, "a number of drugs have been put on the market with efficacy claims based on extremely meager and unobjective observations"); *id.* at 176-77 (quoting Dr. Frederick Meyers, "Much of what passes as clinical investigation . . . is really an effort to get the drug used in a medical center before general release, to get a physician of some influence to use the drug as part of a clinical trial . . . .").

After 1962, the National Academy of Sciences found that adequate effectiveness information was lacking for eighty percent of the approximately 16,000 promoted uses of drugs. R. Wilson, Center for Drugs and Biologics, FDA, *The DESI Program: A Landmark Accomplishment in Public Health,* Presented at the 8th Annual Meeting of the Regulatory Affairs Professionals Soc'y (Sept. 13, 1984).

[46] S. REP. NO. 448, *supra* note 8, at 204.

[47] *See* Bates v. State Bar of Arizona*,* 433 U.S. 350, 366 (1976) (expressing concern about the misleading nature of advertising claims relating to the quality of legal services); Zauderer v. Office of Legal Counsel*,* 471 U.S. 626, 641 n.9 (1985) ("our decisions have left open the possibility that States may prevent attorneys from making non-verifiable claims regarding the quality of their services").

[48] K. Dickersin & Y.I. Min, *NIH Clinical Trials and Publication Bias*, ON-LINE J. CURRENT CLIN. TRIALS, Apr. 28, 1993, at Doc. No. 50.

[49] J.E. Bekelman, Y. Li & C.P. Gross, *Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review*, 289 JAMA 454-65 (2003); J. Lexchin et al., *Pharmaceutical Industry Sponsorship and Research Outcome and Quality: Systematic Review*, 326 BRITISH MED. J. 1167-70 (2003); F. Davidoff et al.*, Sponsorship, Authorship, and Accountability,* 286 JAMA 1232-34 (2001).

reported studies in peer-reviewed literature rarely themselves put the results of the reported study in the context of other relevant research.[50] It would be naïve to suggest that widespread dissemination of positive findings to physicians by the pharmaceutical industry's 86,000 drug representatives will somehow be balanced and put into a fair and accurate context by other sources.

There is, in addition, the troubling reality that our system of peer-review hardly is a guarantee that data are unbiased or reliable. A recent review of fifty systematic reviews and meta-analyses on the treatment of asthma, including thirty-eight peer-reviewed articles, found that forty of these had "serious or extensive flaws," including all six of the reviews funded by the pharmaceutical industry.[51] The authors concluded, "*most reviews published in peer reviewed journals or funded by industry have serious methodological flaws that limit their value to guide decisions*."[52] Unfortunately, if these flaws were not evident to the peer-reviewers, they certainly will not be evident to the average physician. And yet, because these are "peer-reviewed" articles, physicians will give them special weight.

Experts share the doubts about the usefulness of peer-review in ensuring the reliability of reported data. The editor of *The Lancet*, noting that the *The Lancet* and the Royal Society's peer-review processes recently had come to opposite conclusions about the reliability of an important study, wrote in the *Medical Journal of Australia*, that "the system of peer review is biased . . . [and] frequently wrong."[53] A review by the prestigious Cochrane Collaboration of studies on the value of the peer-review process concluded, "At present, there is little empirical evidence to support the use of editorial peer review as a mechanism to ensure quality of biomedical research, despite its widespread use and costs."[54] Even more troubling, the editors of eleven prestigious peer-reviewed medical journals recently wrote of their serious concern about the growing number of published studies in which the corporate sponsor rather than the investigator dictated study design, analysis, and reporting. According to the authors, such practices "not only erode the fabric of intellectual inquiry that has fostered so much high-quality clinical research, but also make medical journals party to potential misrepresentation . . . ."[55] And an editorial in *Nature* warned against over-reliance on peer-reviewed publications, arguing that there was a need for "independent assessment and, in the midst of controversies, publicly funded agencies providing comprehensive, reliable and prompt complementary information."[56]

There is little basis to believe that dissemination of peer-reviewed studies or textbooks by pharmaceutical companies is significantly less misleading than other forms of promotion. Nor can industry-initiated dissemination of peer-reviewed articles substitute for independent review of a product's safety and effectiveness by FDA. The system of peer-review cannot satisfy the substantial government interest in assuring that marketed drugs are safe and effective because the universe of peer-reviewed data has a fundamental limitation: it includes data only on what people have chosen voluntarily to

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[50] M. Clarke et al., *Discussion Sections in Reports of Controlled Trials Published in General Medical Journals,* 287 JAMA 2799-2801 (2002).

[51] A.R. Jadad et al., *Systematic Reviews and Meta-Analyses on Treatment of Asthma: Critical Evaluation*, 320 BRITISH MED. J. 537-40 (2000).

[52] *Id.*

[53] R. Horton, *Editorial, Genetically Modified Food: Consternation, Confusion, and Crack-up*, 172 MED. J. AUSTRALIA 148-49 (2000).

[54] T.O. Jefferson et al., *Editorial, Peer-Review for Improving the Quality of Reports of Biomedical Studies*, 1 THE COCHRANE LIBRARY (2003).

[55] Davidoff et al., *supra* note 49, at 1232-34.

[56] *Editorial, Dangers of Over-Dependence on Peer-Reviewed Publication*, 401 NATURE 727 (1999).

study. Only FDA review *requires* that there be sufficient data to establish safety and effectiveness for each use of each product.

D. *Other Restrictions Shown to Be Inadequate to Prevent Harm*

FDA has suggested that rules against false and misleading claims and/or disclaimers could provide adequate protection to consumers from dangerous and deceptive products, and that prohibiting the promotion of unapproved uses is, therefore, unconstitutional. To the contrary, Congress had more than enough evidence to demonstrate that neither of these methods could protect consumers.

When Congress imposed effectiveness requirements on drugs and devices, it had abundant evidence that a rule against false and misleading advertising coupled with postmarket enforcement actions was ineffective in protecting consumers from harm. As described above, the major thrust of five years of hearings was a demonstration that this very regulatory regime failed to stop the promotion of deceptive and dangerous products.[57] As one public health expert testified:

> It is not sufficient to say that some law in some book presently forbids some of these practices. Long before governmental authorities are in a position to prove the illegality of these practices and get the cumbersome legal machinery into motion and remove the drug from the market, grave harm has been done.
>
> This evil can only be remedied, we believe, in a fair and practical way by putting the burden where it belongs, on the manufacturers of these potent drugs, by requiring them to demonstrate the efficacy and safety of their products.[58]

The Secretary of HEW, too, testified that the absence of an effectiveness requirement left consumers unprotected from harmful products and that reliance on postmarket actions against misleading advertising had proven itself to be "indefensible":

> Even if the FDA has reason to believe that [a] new drug is not effective for the purposes claimed, it must approve the new drug application once the requirements of safety have been met. Then the manufacturer is at liberty to promote his product. If claims for effectiveness are made which the FDA believes are groundless, a proceeding must then be brought to take the drug off the market as a misbranded product. At that point the burden of proof is on the FDA to establish that the drug is not effective. And throughout the period of time it takes for the FDA to prepare its case and secure relief in the courts, the manufacturer will have foisted his product upon an unsuspecting public.

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[57] *Drug Industry Act of 1962 Hearings*, *supra* note 8, at 63 (statement of Abraham Ribicoff, Sec'y of HEW); *id.* at 463-64 (statement of Andrew J. Biemiller, Dir., Dep't of Legislation, AFL-CIO, and former Congressman) (FTC's attempts to correct false advertising of Doan's pills took several years); *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 171 (statement of Abraham Ribicoff, Sec'y of HEW); *id.* at 66-68, 71 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health); *id.* at 102-03 (statement of Dr. Harold Book, Dir. of Labs., Norristown State Hosp., and Ass't Prof. of Neuropathology, Grad. School of Med., Univ. of Pa.); *Weight Reducing Preparations Hearings*, *supra* note 8, at 42 (statement of Maye Russ, Nat'l Better Business Bureau); *id.* at 197-212 (FTC table showing lengthy period of time between initiation of investigation of deceptive claims and final cease and desist orders).

[58] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 66-68 (statement of Dr. Leona Baumgartner, Comm'r, N.Y. City Dep't of Health).

> [W]e believe that where public health is involved it is intolerable to permit the marketing of worthless products under the rules of a cat-and-mouse game where a manufacturer can fool the public until the Food and Drug Administration finally catches up with him.[59]

FDA also suggests that disclaimers might be adequate replacements for a demonstration of safety or effectiveness. The record before Congress is more than sufficient to demonstrate that disclaimers cannot broadly protect consumers from unsafe and ineffective products to improve health. A disclaimer could take many forms, but the two most obvious forms are 1) a required statement that the government has not reviewed the claim; and 2) a statement created by the manufacturer ostensibly providing adequate information for a consumer to assess the weight of the evidence supporting a claim (e.g., "some studies suggest that this product is effective while others are inconclusive"). In a variation of the second type of disclaimer, FDA might issue a regulation specifying types of information that must be in a disclaimer or specifying other details of presentation. The drafting of specific disclaimers would still be the responsibility of the manufacturer, and, in the absence of premarket review of claims, FDA would still be required to initiate an enforcement action if it believed the disclaimer violated the regulation or was otherwise misleading.

The first type of disclaimer would provide precisely the information known to every physician before 1962: at that time, as everyone knew, the government did not review the effectiveness of drugs. This knowledge, however, did not in any way assist physicians in determining which products would help their patients and which would not, because that information generally was unavailable in a system where no one was required to establish effectiveness.[60] Thus, a disclaimer stating that a claim had not been reviewed by FDA would provide no useful information to a physician about whether to prescribe the drug and would offer patients no protection from unsafe or ineffective products, or from the harm that can flow from such products.

The second type of disclaimer relies on the manufacturer to disclose the true state of the scientific evidence supporting a claim. Once again, when there is little reliable evidence to support a claim, a disclaimer, no matter how truthful, cannot help physicians determine which products will provide treatment for their patients and which will not. The harm that flows from a marketplace in which there is little reliable evidence on the effectiveness of the products physicians must prescribe for their patients was described in great detail in the Congressional hearings preceding the 1962 Amendments to the FDCA.

Moreover, both those hearings, and subsequent hearings on drug advertising, repeatedly showed that, in the absence of government review, many companies fail to provide, in promotional material, an objective presentation of the evidence supporting their products.[61]

To those who would argue that the marketplace has changed since 1962, there are two responses. First, the gains that have been made are a result of the rigorous regulation that produces adequate studies and restricts irresponsible promotion. The world of dietary supplement claims provides ample evidence of what happens when claims are deregulated. Second, there is ample evidence that information provided to doctors by

[59] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 173 (statement of Abraham Ribicoff).

[60] *Drug Industry Antitrust Act Hearings*, *supra* note 8, at 105-06 (statement of Dr. Harold Book, Dir. of Labs., Norristown State Hosp., and Ass't Prof. of Neuropathology, Grad. School of Med., Univ. of. Pa.); S. REP. NO. 448, *supra* note 8, at 203 (quoting Dr. Louis Lasagna); *id.* at 187 (quoting Dr. Dowling); *id.* at 176-77 (quoting Dr. Frederick Meyers).

[61] *Competitive Problems in the Drug Industry, Summary and Analysis of Hearings Before the Select Comm. on Small Business, Subcomm. on Monopoly, U.S. Senate*, 92d Cong., 2d Sess. (1972).

pharmaceutical companies continues to lack objectivity.[62] There is no more reason to expect these companies to provide a truthful, nonmisleading disclaimer than there is to expect that the promotional claims themselves will be truthful and nonmisleading.

III. CONCLUSION

Our country's long-standing requirements that medical products be shown to be safe and effective before marketing are well-justified. They are supported by decades of experience and thousands of pages of congressional documents showing the grave harm to the public health that follows unrestricted promotion of health-related products.

FDA has suggested that there may be a case for ceasing to enforce many of the promotional restrictions of the FDCA. The agency apparently is contemplating this action because its current leadership believes that, under the First Amendment, the only way the agency may protect the public health is to trust the pharmaceutical industry not to make deceptive or dangerous promotional claims about its products. This conclusion is unsound as a matter of law, and disastrous as a matter of public policy. The detailed record of past abuses by those marketing products to improve health is more than sufficient to justify the constitutionality of the current protections. These restrictions were enacted to prevent repetition of real harm to American lives and were based on evidence that lesser restrictions had failed to prevent these harms. FDA has no basis under the First Amendment for failing to enforce the current limitations on the promotion of health-related claims.

If there has been any lesson learned in the last two years from the accumulation of corporate accounting scandals, it is that even some of the largest and most successful corporations in America are capable of abusing the public trust. When corporate wrongdoers placed short-term profits ahead of the truth in accounting, millions of Americans lost their jobs and their savings. If some of our most important requirements on promotion of products to improve health are removed, and corporations do not live up to their obligation to promote those products objectively and truthfully, many Americans could lose their lives.

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[62] *See, e.g.*, M. Wilkes et al., *Pharmaceutical Advertisements in Leading Medical Journals: Experts' Assessments*, ANNALS INTERNAL MED. 912-19 (June 1, 1992) ("In 44% of the cases, reviewers felt that the advertisement would lead to improper prescribing if a physician had no other information about the drug other than that contained in the advertisement."); Gutknecht, *Evidence-Based Advertising? A Survey of Four Major Journals*, J. AM. BOARD FAMILY PRACTICE, 197-200 (May-June 2001) ("Descriptions of research in pharmaceutical advertisements were brief and incomplete, and they inconsistently provided the basic design and statistical information needed to judge the results reported."); *Madison Ave. Plays Growing Role in Drug Research*, N.Y. TIMES, Nov. 22, 2002 (advertising agencies hired by drug companies are increasingly conducting their own clinical trials to use in promotion of drugs).