2000

Drug and Device Litigation in the 21st Century

Linda S. Syitak

Peter J. Goss

Follow this and additional works at: http://open.mitchellhamline.edu/wmlr

Recommended Citation

Available at: http://open.mitchellhamline.edu/wmlr/vol27/iss1/25
DRUG AND DEVICE LITIGATION IN THE 21ST CENTURY

Linda S. Svitak†
Peter J. Goss‡

I. INTRODUCTION .............................................................. 272
II. ONLINE PHARMACEUTICAL SALES ..................................... 272
   A. Regulatory Overview .................................................. 273
   B. The Absence Of A "Learned Intermediary" ......................... 274
   C. Illegal Off-Shore Drug Sales ......................................... 276
   D. Privacy ....................................................................... 278
III. DIRECT-TO-CONSUMER ADVERTISING: DEATH-KNELL FOR THE LEARNED INTERMEDIARY DOCTRINE? ............... 279
   A. Regulatory Requirements .............................................. 279
   B. Implications Of Direct Advertising For The Learned Intermediary Doctrine .................................................. 281
       1. Some Courts Consider DTC Advertising Another Exception To The Learned Intermediary Doctrine ..................... 282
       2. Despite These Holdings, The Learned Intermediary Doctrine Is Still Alive In Most Jurisdictions ......................... 284
   C. A Related Issue: "Med Guides" .................................... 285
IV. DISSEMINATING INFORMATION ON OFF-LABEL USES: ILLEGAL PROMOTION, OR FREE SPEECH? ....................... 285
   A. Round 1: Washington Legal Foundation vs. Friedman .............. 286
   B. Round 2: Washington Legal Foundation vs. Henney .............. 288
   C. Round 3: FDA Retreats-And Wins? ................................ 288
V. INDUSTRY GIFTS TO PHYSICIANS: SUPPORTING INNOVATION OR "BUYING SCIENCE?" ........................................ 290
   A. Influence In Practice: The Jama Study On Physician Gifts

† B.A., B.S.N., St. Olaf College, J.D., William Mitchell College of Law. Ms. Svitak is a Partner in the Minneapolis office of Faegre & Benson LLP, and practices in drug and medical device products liability defense.
‡‡ B.A., M.A., J.D., University of California, Berkeley. Mr. Goss is an Associate in the Minneapolis office of Faegre & Benson LLP, and practices in drug and medical device products liability defense.
The last half of the 20th Century saw the emergence of the "medical mass tort" as a legal construct, a media opportunity, and a staple for products liability litigators. Drug and device litigation spawned innovations in the law as it grappled with the complex issues presented by each new product; market-share liability (DES litigation),1 Daubert challenges (Bendectin litigation),2 and court-appointed science panels (breast implant litigation)3 are just a few examples. But the issues faced by medical manufacturers in this Century promise to be as interesting and as challenging as those of the past. Patient privacy, marketing and promotional practices, physician-industry conflicts of interest, the continuing evolution of the learned intermediary doctrine, and reuse of "single-use" medical devices will be among the major themes of drug and device litigation in the future.

II. ONLINE PHARMACEUTICAL SALES

The boom in e-commerce has generated expanded consumer demand for prescription drugs over the internet. The convenience of home delivery, along with the discounts offered by many pharmacy sites, make online purchasing very appealing.4 Among the benefits of online medication purchasing are:

—greater availability of drugs for shut-in people or those who do not live near a pharmacy

—comparative shopping among sites in order to find the lowest prices

—greater convenience and a larger variety of products

—greater, faster access to written information relating to

medications
—the privacy of buying medical products from home.\footnote{5}

But the increased volume of online drug buying raises concerns over the privacy of patient medical information, the physician's involvement (if any) in a patient's medication decisions, and—as "rogue" sites selling "prescription-free" drugs proliferate—the regulatory and legal compliance of suppliers.

\textbf{A. Regulatory Overview}

Enforcement of the laws and regulations that apply to online pharmacies involves a tangle of state and federal agencies.\footnote{6} Pharmacies have traditionally been regulated by the states,\footnote{7} but the internet exceeds the reach of any one state's laws; while state agencies can seek to enjoin online sites from doing business in their state, they still remain open for business in the other 49 states. Further, while more scrupulous sites like Drugstore.com have obtained pharmacy licenses in all 50 states,\footnote{8} others are licensed in just one—but sell to all comers, in whatever state they reside. To avoid charges of practicing medicine and dispensing drugs without a license in the other states, these sites argue that a customer, by visiting the site, actually enters the state where the site is licensed.\footnote{9} This argument has yet to be tested in court, however.

Given the limited powers of the state agencies, the FDA and the Federal Trade Commission play key roles at the national level by regulating drug claims and enforcing the Food, Drug, and Cosmetic act.\footnote{10} Customs and the Postal Service also help regulate shipments of drug products.\footnote{11} But regulating Internet pharmacy sites, as an online seller of Viagra put it, is "kind of like trying to nail Jell-O to a wall."\footnote{12} Sites can show up on the Web and then dis-
appear overnight. In many cases, all that is needed to set up an online drugstore is a valid doctor's license, a relationship with a drug wholesaler, and a credit card, making regulatory oversight the equivalent of trying to hold back the ocean with a dike made of sand.  

B. The Absence Of A "Learned Intermediary"

Many of the "online pharmacies" only require purchasers to fill out a questionnaire to obtain medications, bypassing the traditional requirement of a physician's prescription. Such sites usually claim that questionnaires are reviewed by a doctor—but rarely is any information provided about who the doctor is and what his or her credentials are. 14 Most of the time, patients do not learn who their doctors are until the drugs arrive in the mail. 15 Further, if a consumer is convinced that he or she needs a particular treatment, questionnaire answers may be falsified with relative ease. 16 Thus, while the questionnaire may save a trip to the doctor's office, the time savings is very likely outweighed by the increased risk of harm. According to Jeffrey Shuren, M.D., a medical officer in the FDA's Office of Policy, Planning, and Legislation, "Patients risk obtaining an inappropriate medication and may sacrifice the opportunity for a correct diagnosis or the identification of a contraindication to the drug." 17

An example shows just how grave the consequences can be. In Illinois, a 52-year-old man with a history of chest pains and a family history of heart disease bought Viagra from a site only requiring that he fill out a questionnaire. 18 The man later died of a heart attack. 19 While no connection between the drug and the man's death has been shown, it is nevertheless unlikely that he would have been able to obtain the drug had he seen his doctor, given his cardiac risk factors. 20 This scenario raises the question whether the manu-

13. Id.
17. Id. at 26.
18. Id.
19. Id.
20. Id.
The pharmacy industry has recently undertaken efforts at self-regulation in order to impose accountability and quality assurance on Internet sales of prescription drugs. The National Association of Boards of Pharmacy (NABP) recently introduced a certification program, "Verified Internet Pharmacy Practice Sites" or "VIPPS." Certification under VIPPS requires online pharmacy sites to maintain all their state licenses in good standing, to allow information about them to be posted on the VIPPS website, and to allow inspections by the NABP. The VIPPS certification program is the "carrot" offered by the NABP; but they appear ready to wield the stick if necessary. According to Carmen Catizone, executive director of the organization, "Any site that uses a questionnaire without a legitimate patient-physician relationship, we consider illegal."

The American Medical Association ("AMA") is also taking steps to remedy the lack of standards governing online prescribing. At its June, 1999 annual meeting, the AMA discussed guidelines dealing specifically with Internet prescriptions, which included a requirement that patients first receive an in-person physical examination. Manufacturers voiced support for the AMA's efforts. Martin Hirsch, public affairs director for Roche, makers of Xenical—a popular weight-loss drug frequently sold at sites not requiring a prescription—indicated that "[t]he relationship between physician and patient is critically important" and expressed Roche's support for "guidelines that will ensure that this relationship continues."

Manufacturers are clearly concerned about the liability implications of consumers buying their products without a doctor visit. Not only will the practice result in injuries stemming from inappropriate prescriptions, it will bring increased pressure to provide direct warnings to consumers, where now manufacturers need only warn doctors under the "learned intermediary" doctrine. In August, 1998, when the Viagra craze was in full swing, Pfizer filed a complaint with the Federal Trade Commission alleging that online sites are deceiving consumers by ignoring the label's advice that the

21. Id. at 29.
22. Id.
24. Id.
25. Id.
drug be prescribed only after a physical examination.  

C. Illegal Off-Shore Drug Sales

Recognizing the regulatory slipperiness of online drug sales, the Clinton administration is seeking more Federal oversight of online drugstores. The President is requesting legislation that would require online drug sellers to get FDA approval before transacting sales on the Web. The legislation would also create civil penalties of up to $500,000 for selling drugs without a prescription or without FDA certification. The administration is also seeking $10 million from Congress to beef up its enforcement of online drug sales.

But increased regulation at the Federal level may only result in more sites moving their operations overseas, joining the numerous foreign "pharmacies" already online selling drugs unavailable without a prescription—or unavailable altogether—in the U.S. According to Customs Service Commissioner Raymond W. Kelly, "[a]ny of these internet pharmacies are fly-by-night operations set up overseas to avoid U.S. law. They have little regard for patient safety." Many of the sites also sell products that are either different from those approved in the U.S. or are past their expiration dates. Imported drugs may be especially dangerous, according to one Customs official, because "[a] lot of this stuff is being cooked up in somebody's back room in Thailand" and "may be laced with all sorts of contaminants."

The U.S. and Thai governments recently joined forces to shut down seven prescription-drug-selling web sites operating in Thailand, the first-ever bust of a foreign online drug-selling operation.

29. Id.
30. Id.
34. Id.
One of the Thai sites, Vitality Health Products, advertised "prescription-free pharmaceuticals by e-mail at incredibly low prices" and sold popular drugs like Minoxidil, Propecia, Viagra, Retin-A, and Premarin. The Website even advised customers what to do in the event customs seized their shipment.

The bust, orchestrated by Thai police and the Thai equivalent of the FDA, netted 20 computers, 245 parcels destined for the U.S., and more than 2.5 million pounds of drugs—including anabolic steroids, Valium, Viagra, fen-phen, Tylenol with codeine, and Xanax. But the Thai operations appear to have been the tip of the iceberg. Numerous similar sites continue selling prescription drugs unabated from bases in Mexico, Switzerland, Britain, New Zealand, and elsewhere. Customs seized nearly 10,000 packages containing prescription drugs in 1999, 4.5 times more than in the previous year. The drugs seized either had not been approved in the U.S., did not comply with FDA labeling requirements, or fell below federal standards for the quality and purity of drugs.

Customs acknowledges that the number of pills seized probably represents only a fraction of the total volume of prescription drugs being imported due to Internet sales. Frequently the orders are sent in nondescript packages that do not declare their contents, making detection difficult. And enforcement resources are limited: a spokesman for Customs indicates that the agency usually refrains from taking action when consumers import small amounts of drugs, noting that "[w]e won't arrest Granny just because she wants to get her drugs cheaper."

The illegal sale of expired or contaminated products, often without prescription, may create complex products liability issues for drug manufacturers, such as:

To what extent are manufacturers responsible for injuries suffered by people who obtained their drugs illegally?

Must manufacturers act to shut down such illegal distribution

35. Id.
36. Id.
37. Id.
38. Id. One site, "Direct Response Marketing," runs its operations from the Channel Islands. http://www.directresponsemaking.co.uk/.
40. Id.
41. Id.
42. Id.
channels when they become aware of them?

What liability, if any, does a manufacturer have for injuries resulting from its product when the product has been contaminated or "laced" with another substance by a third party outside normal distribution?

Can the "learned intermediary" defense still be used if there was no intermediary?

Does the manufacturer have a duty to warn these users directly, even though obtaining the drug without a doctor's prescription is illegal?

Courts will increasingly have to confront these thorny questions as illegal on-line sales of prescription drugs continue to grow.

D. Privacy

The confidentiality of private medical information will become a greater concern as more and more prescriptions are filled over the Web. One of the most popular uses of the Internet is for health information, and this has led many web-users to submit personal medical information to unsecured chat-rooms and health-related sites. In addition, doctors and patients are increasingly communicating by e-mail; hospitals are providing patients access to their medical records on-line; and some health plans are even enrolling new members over the Internet. While many of the larger sites use secure servers and encrypt personal information, more marginal sites do not. In this manner, personal health information can become accessible to insurance companies, would-be employers, and others who could use it to their advantage.

Of particular concern with respect to online drug purchases are "cookies," which many retail websites use to track the buying habits of visitors to their sites. While "cookies" can provide consumers the convenience of information and products tailored to their interests, and eliminate the need for a log-in with every visit to the site, they could also show that a customer was buying a particular drug on a continuing basis. In this manner, a customer's buying habits could reveal that he has the virus that causes AIDS, or suffers from depression, impotence, or any number of other conditions he

43. Milt Freudenheim, Privacy a Concern as Medical Industry Turns to Internet, N.Y. Times, August 12, 1998.
44. Id.
45. Margaret A. Winkler, M.D., et al., Guidelines for Medical and Health Information Sites on the Internet, 283 JAMA 1600, 1605 (2000).
would rather have kept private.\textsuperscript{46}

Privacy issues do not present a significant liability concern for drug and device manufacturers, who are usually blind to the identities of end-users of their products. Retailers, however, could end up paying steep damages awards if they seek to profit from the sale of confidential medical information, or otherwise fail to protect the privacy of their customers.

III. DIRECT-TO-CONSUMER ADVERTISING: DEATH-KNELL FOR THE LEARNED INTERMEDIARY DOCTRINE?

Relationships among healthcare manufacturers, doctors, patients, and payers have been transformed in recent years by increased competition, the cost-sensitivities of managed care, and growing patient involvement in health care decisions. In particular, the old hierarchy for communicating information about prescription drugs—from manufacturer to doctor to patient—is being subverted. In the era of managed care, physicians no longer control demand for prescription drugs to the degree they once did; they must answer to their employers and to payers, who often are reluctant to try new products—particularly if the cost of the new treatment is higher than its predecessor. Therefore, recognizing that consumers are more than ever driving the demand for prescription drugs, manufacturers are increasingly promoting their products directly to public and bypassing the "filter" traditionally applied by the medical community.

A. Regulatory Requirements

FDA regulates prescription drug advertising for the accuracy and adequacy of their content.\textsuperscript{47} While accuracy is a relatively straightforward requirement, adequacy can be more complex. The Food, Drug and Cosmetic Act requires that advertisements for prescription drugs include information "in brief summary" relating to side effects, contraindications, and effectiveness of the drug.\textsuperscript{48} By the time a manufacturer has complied, however, the summary is often far from brief. Other code provisions direct that the brief summary must disclose side effects, contraindications, warnings,
and precautions under the headings "cautions," "special considerations," "important notes," and "effectiveness." At the end of the day, the "brief summary" generally must include all of the language contained in the product's package insert.

This language, commonly provided in eye-straining "mouse-print," is lengthy, technical, and detailed to the point of incomprehension for the average layperson. In fact, the technical nature of this language is one of the main reasons for the learned intermediary rule—only a physician is properly qualified to understand, digest, and translate such highly technical information in terms her patients can understand.

The regulations for advertising prescription drugs through broadcast audio such as television or radio modify the disclosure requirements. Recognizing that the length of a "brief summary" would make radio and television advertising impossible, FDA limited the disclosure requirements in the broadcast media to a "major statement" of the risks attendant to the therapy. Also, in lieu of presenting a "brief summary" in connection with the ad, a sponsor may provide a way for the viewer to obtain the approved package labeling outside the broadcast presentation. This alternative is known as "the adequate provision" requirement.

While the adequate provision requirement made broadcast advertising more accessible to drug and device manufacturers on paper, manufacturers did not seize the opportunity because FDA was silent on how the requirement could be satisfied. Without some assurances from the agency, manufacturers found the risk that their advertising would be found in violation of the FDCA—which would lead their product to be considered "misbranded" and subject to seizure—were simply too great.

Thus, in August of 1997, FDA addressed manufacturers' fears by publishing a draft guidance entitled "Consumer-Directed Broadcast Advertisements," which sets out criteria for the "adequate provision" of labeling information. The agency issued the final guidance, which does not differ substantially from the draft, on

52. Id.
In the guidance suggests a four-part approach:

1. The ad should include a toll-free telephone number for consumers to call for the approved package labeling. Following their call, consumers should be given the choice of receiving the labeling by mail, fax, or by having it read to them over the phone.

2. The ad should indicate that additional product information is available in print advertisements or brochures. This provides a mechanism for consumers who do not have internet access to obtain the labeling. Thus, the broadcast ad could refer consumers to a print ad containing a "brief summary," or direct them to brochures available at doctors' offices, libraries, and pharmacies.

3. The ad should state that pharmacists and/or physicians may provide additional product information to consumers.

4. The ad should provide an internet address, either during the broadcast or through the toll-free number, where consumers can access the labeling.

An ad containing these elements should meet the "adequate provision" requirement, assuming it also includes a thorough "major statement" conveying the product's most significant risks.

B. Implications Of Direct Advertising For The Learned Intermediary Doctrine

In the old marketing regime, prescription products were only marketed to physicians, and only physicians received warnings information about the product. This was consistent with the principles underlying the learned intermediary doctrine, through which a manufacturer discharges its duty to warn by informing physicians—and not health-care consumers—of risks associated with the medication. Where products are the subject of direct advertising, however, the applicability of these principles is called into question.

The learned intermediary doctrine assumes that consumers

---

55. Id. at 2.
56. Id.
57. Id. at 2-3
58. Id. at 2.
must have a doctor navigate them through the complex medical and scientific issues presented by prescription drug treatment. Thus, the manufacturer's duty is limited to providing adequate warnings to the physician, who has a corresponding duty to translate that information in terms that her patients will understand.

Exceptions to the doctrine have emerged over the years with respect to mass immunizations, oral contraceptives, and Intrauterine contraceptive devices (IUDs).\(^60\) Courts have reasoned that since mass immunizations are not usually administered by physicians, little specialized information is conveyed to the patient, and therefore manufacturers must warn consumers directly of any risks.\(^61\) With respect to oral contraceptives and IUDs, courts have held that since patients ultimately decide for themselves which form of birth control to use, they must be warned directly in that instance as well.\(^62\)

The rationale behind each of these exceptions is that the consumer, and not the physician, ultimately drives the decision whether to obtain the product, and that the doctor's role in providing specialized information is diminished. This rationale is cited in support of arguments that manufacturers lose the learned intermediary defense when they engage in direct-to-consumer advertising.

1. Some Courts Consider DTC Advertising Another Exception To The Learned Intermediary Doctrine

*Edwards v. Basel Pharmaceuticals*\(^63\) is an example of a case where the court held DTC advertising was an exception to the learned intermediary doctrine. In *Edwards*, the decedent suffered a fatal heart attack which allegedly resulted from overuse of a nicotine patch. The package insert specifically disclosed the risk of death from overdose, but the direct-to-patient warnings did not. The manufacturer asserted that, consistent with the learned intermediary doctrine, its liability for failure-to-warn could only be assessed with respect to the physician-directed package insert.

The Oklahoma Supreme Court disagreed. Despite the full warning in the package insert, the court held that:

---

60. *Id.*
61. *Id.*
62. *Id.*
63. 933 P.2d 298 (Okla. 1997).
When direct warnings to the user of a prescription drug has been mandated by a safety regulation promulgated for the protection of the user, an exception of the learned intermediary doctrine exists, and failure on the part of the manufacturer to warn the consumer can render the drug unreasonably dangerous.\textsuperscript{64}

In \textit{Shanks v. Upjohn Co.},\textsuperscript{65} a case involving the drug Xanax, the court held that prescription products where patients initiate the usage, where drugs are typically administered in a clinical setting with little patient input or where drugs marketed under a strategy designed to appeal directly to the consuming public are areas where courts have held that manufacturers have a duty to warn patients directly.\textsuperscript{66}

In \textit{In Re Norplant Contraceptive Products Liability Litigation},\textsuperscript{67} a federal court in Texas held that the defendant's direct advertising campaign for Norplant, an implantable contraceptive, did not eliminate the learned intermediary defense because the plaintiffs never saw any of the ads before receiving their implants. But the court did not address the question "[w]hether a drug manufacturer's use of direct-to-consumer advertising is ever grounds for creating an exception to the learned intermediary doctrine," indicating that "This is an issue which should be resolved by the Texas Supreme Court."\textsuperscript{68}

Finally, in another Norplant case, \textit{Perez v. Wyeth Laboratories, Inc.},\textsuperscript{69} the New Jersey Supreme Court held that direct-to-consumer advertising creates an exception to the learned intermediary rule. The Court expressed its view that "Our medical-legal jurisprudence is based on images of health care that no longer exist" in ruling that the underpinnings of the learned intermediary doctrine are absent in the context of consumer-directed advertising.\textsuperscript{70} Unlike in the past, doctors have less time to discuss risks with patients, and drug companies have much greater access to consumers through direct advertising; therefore, the Court reasoned, manufacturers should be held liable if their advertising fails to provide adequate

\textsuperscript{64} Id.
\textsuperscript{65} 835 P.2d 1189 (Alaska 1992).
\textsuperscript{66} Id. at 1195, n.7.
\textsuperscript{67} 955 F. Supp 700 (E.D. Tex. 1997).
\textsuperscript{68} Id. at 708, n. 45 (emphasis added).
\textsuperscript{69} 734 A.2d 1245 (N.J. 1999).
\textsuperscript{70} Id. at 1246, 1255.
warnings.  

The Court did suggest, however, that compliance with FDA regulations governing consumer-directed advertising would be a defense to a failure-to-warn claim.

2. Despite These Holdings, The Learned Intermediary Doctrine Is Still Alive In Most Jurisdictions

In Polley v. Ciba-Geigy Corporation, a federal court in Alaska applied the learned intermediary doctrine despite direct communications in patient brochures. The court held that the brochures did not create an exception to the learned intermediary rule. Mikell v. Hoffman-LaRoche, Inc. held similarly. There, an informational pamphlet identifying some, but not all risks associated with the drug Accutane did not void the learned intermediary defense since the plaintiff's prescribing physician was aware of the risk when he wrote the prescription.

In Presto v. Sandoz Pharmaceuticals Corporation, the Georgia Court of Appeals concluded that a pamphlet entitled, "Understanding Clozaril (Clozapine) Therapy: A Guide For Patients And Their Families," did not nullify the learned intermediary doctrine because the plaintiffs could not have reasonably relied on the pamphlet for warnings concerning the dangers of the use of Clozaril. According to the court, "[t]he pamphlet does not constitute an effort to inform patients of all the dangers of Clozaril and does not purport to do so....The booklet states that it 'provides answers to many questions about Clozaril' but cautions the reader 'if there are other questions about Clozaril therapy, be sure to ask the doctor, nurse or pharmacist.'"

These decisions seem more in tune with health-care decision-making today. Even with the increase in information available directly, consumers still need a doctor to balance the benefits against the risks and to provide expert advice on whether the therapy is appropriate. While direct advertising creates a more educated public, it can never replace the particularized information that physicians provide, and it therefore should not relieve doctors of their duty to inform their patients.

71. Id. at 1255-57.
72. Id. at 1259.
75. 487 S.E.2d 70 (Ga. 1997).
76. Id. at 74.
C. A Related Issue: "Med Guides"

The issue of manufacturers' responsibility to provide warnings to consumers arose before the ascendance of direct-to-consumer advertising. In 1995, FDA proposed a rule that would require manufacturers to produce "med guides" for their products, along the lines of the "Nutrition Facts" labeling provided on food products. In 1997, Congress rejected the comprehensive plan. But FDA has recently gone forward with a less ambitious plan to require such guides for 10 drugs it considers particularly dangerous in a given year. Further, under new Department of Health and Human Services regulations, 75% of all prescriptions must come with leaflets containing "useful information" by the end of 2000, and 95% by 2006—otherwise, FDA promises to reintroduce its med guides plan.

As doctors, under pressure from managed care payers, have less and less time to discuss risks of medications with their patients, Congress may have no choice but to adopt the program the next time around. Clearly, the consequences would be grave for the learned intermediary doctrine.

IV. DISSEMINATING INFORMATION ON OFF-LABEL USES: ILLEGAL PROMOTION, OR FREE SPEECH?

The increased volume of drug and medical device advertising belies the fact that medical products marketing is often a regulatory high-wire act. When FDA approves a medical device or pharmaceutical, it allows sale of the product for the approved indications and for those indications only. Thus, although doctors frequently discover new and highly beneficial uses of approved products, drug and device companies are not allowed to market the products for those uses without going through the FDA approval process all over

77. 60 FR 44181 (August 24, 1995); see also Sheryl Gay Stolberg, FDA Pushes for Prescription Drug Guides, N.Y. Times, June 4, 1999.
78. Stolberg, supra note 77.
79. Id.
80. Id.
81. Id.
Doctors, however, remain free to prescribe medication for unapproved uses, a practice known as "off-label use." For example, doctors for years have prescribed aspirin in order to reduce the risk of heart attacks, but this "off-label" use was not actually approved by FDA until 1998. The pharmaceutical industry estimates that anywhere from 25% to 60% of the 1.6 billion prescriptions written annually are for off-label uses.

Sometimes doctors who discover such beneficial "off-label" uses publish their results, so that others in the health care community may benefit. But when a manufacturer provides a doctor with such articles, is the manufacturer "promoting" its product for the off-label use? Or is the manufacturer merely exercising its free-speech right to provide the doctor with truthful information?

A. Round 1: Washington Legal Foundation vs. Friedman

For the last five years, FDA has taken a strict stance that a manufacturer's mere distribution of information on off-label uses—even without any endorsement or comment of any sort—constitutes illegal marketing and renders the product in question "misbranded." It took this stance in three separate publications:

—Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data, 61 FR 52800 (October 8, 1996);
—Guidance for Industry Funded Dissemination of Reference Texts, 61 FR 52800 (October 8, 1996); and

In Washington Legal Found. v. Friedman, the Washington Legal Foundation ("WLF"), a non-profit organization favoring reduced government regulation, sued the Agency on the ground that the three guidance documents infringed on drug and device manufacturers' First Amendment rights.

WLF argued that the speech in question concerned academic and scientific research, and was therefore entitled to the highest First Amendment protection; the FDA responded that the guid-

82. 21 U.S.C. § 321(p).
83. 59 FR 59820-21 (November 18, 1994).
85. Id.
87. Id.
ances did not implicate the First Amendment, but if they did, the speech at issue was "commercial" and should not be granted the protection of "pure" speech. First, the Court held that the guidelines did constitute speech meriting some level of protection, notwithstanding FDA's argument that its broad regulatory authority empowered it to regulate without running afoul of the First Amendment. Then, while recognizing that the dissemination of off-label use information is "one of those complex mixtures of commercial and non-commercial elements," the court found the manufacturers' activities essentially promotional and worthy of only the qualified protection afforded commercial speech under Central Hudson Gas v. Public Service Comm'n of New York. 447 U.S. 557 (1980). Applying the Central Hudson Gas test, Judge Lamberth held:

1) that dissemination of off-label information is neither unlawful nor inherently misleading;  
2) that the government has a substantial interest in protecting the health of its citizens and in requiring manufacturers to submit off-label uses for FDA approval;  
3) that the guidance documents advance the government's substantial interests; but  
4) that the guidance documents are unconstitutional because they are more extensive than necessary.

Thus, the court found that "[t]hrough the government's well-intentioned efforts to prevent misleading information from being communicated, a great deal of truthful information will also be embargoed." According to Judge Lamberth, an "obvious" and less restrictive alternative to the Continuing Medical Education ("CME") guidances—which would have prohibited manufacturers from distributing articles on off-label topics—is to allow the distribution but with "full, complete, and unambiguous disclosure by the manufacturer" that the materials concern an off-label use. Based on this reasoning, he issued an injunction barring FDA from limiting "any pharmaceutical or medical device manufacturer or any other person":

88. Id. at 59.  
89. WLF I at 59-61.  
90. Id. at 62-65 (citations omitted).  
91. Id. at 65-74.  
92. Id. at 73.  
93. Id.
...from disseminating or redistributing to physicians or other medical professionals any article concerning prescription drugs or medical devices previously published in a bona fide peer-reviewed professional journal, regardless of whether such article includes a significant or exclusive focus on uses of drugs or medical devices other than those approved by FDA...\(^94\)

B. **Round 2: Washington Legal Foundation vs. Henney\(^95\)**

The Guidance documents at issue in *WLF I* were superseded by the passage of the Food and Drug Modernization Act of 1997 ("FDAMA"), which contains specific provisions governing manufacturer distribution of information on off-label uses. Since the FDAMA came into effect after Judge Lamberth issued his injunction, FDA argued that the injunction should be modified to exclude FDAMA and its implementing regulations from the injunction's scope. The Judge instead amended the injunction to clarify that the FDAMA provisions and related regulations, which were essentially the same as the three guidance documents at issue before, were also unconstitutional.\(^96\)

One subtle change instituted by the FDAMA was to permit manufacturers to distribute off-label information, so long as they made an application to FDA to have the use approved within a short time of the distribution. But Judge Lamberth hardly agreed that this removed the taint from the statute:

> The supplemental application requirement of the act amounts to a kind of constitutional blackmail—comply with the statute or sacrifice your First Amendment rights. It should go without saying that this tactic cannot survive judicial scrutiny.\(^97\)

Thus, he concluded that the injunction should not be curtailed, but rather expanded to include the FDAMA and its implementing regulations.\(^98\)

C. **Round 3: FDA Retreats – And Wins?**

By what some would consider a legal Houdini-act, FDA man-

---

94. *Id.*
95. 56 F. Supp. 2d 81 (D.D.C. 1999) (hereinafter "WLF II").
96. *Id.* at 82.
97. *Id.* at 87.
98. *Id.* at 88.
aged to escape the full impact of Judge Lamberth’s decisions and injunctions in \textit{WLF I} and \textit{WLF II} at the Court of Appeals. In argument before the D.C. Circuit, the Agency essentially stipulated that the FDAMA, along with its guidance on industry-supported CME, did not provide it with independent authority to prohibit dissemination of information about off-label uses of drugs and medical devices. The Court of Appeals therefore found, and WLF agreed, that there was no longer a First Amendment issue to be decided, and vacated Judge Lamberth’s decisions and injunctions in \textit{WLF I} and \textit{II} to the extent they declared FDAMA and the CME guidance unconstitutional.\footnote{Washington Legal Found. vs. Henney, 202 F.3d 331 (D.C. Cir. 2000).} In partly vacating the district court’s orders, the D.C. Circuit made it clear that "[w]e certainly do not criticize the reasoning or conclusions of the district court...we do not reach the merits of the district court’s First Amendment holdings and part of its injunction still stands."\footnote{\textit{Id.} at 336.} What the Court did not make clear, though, is which part of the injunction remains standing.

FDA did not "fall on its sword" before the Court of Appeals for no reason. It is now apparent that the agency conceded that FDAMA and the CME guidance do not independently allow speech restrictions in order to preserve a foothold, however tenuous, for maintaining regulatory authority over information about off-label uses. Thus, in spite of the Appeals Court’s approbation\footnote{\textit{Id.}} (albeit in \textit{dicta}) of Judge Lamberth’s reasoning, the Agency remains loyal to its original position, insofar as it intends to use non-compliance with FDAMA and the CME guidance as evidence in "misbranding" actions against manufacturers. The D.C. Circuit’s opinion supports the agency’s authority to proceed in this manner, holding that "[t]he FDA retains the prerogative to use both types of arguably promotional conduct as evidence in a misbranding or 'intended use' enforcement action."\footnote{\textit{Id.}} Consequently, even though the agency may not be able to prevent manufacturers from distributing information about off-label uses, it may still argue that such distribution indicates an intent to promote a use other than the uses in the approved labeling—unless, of course, the distribution falls within the boundaries established by FDAMA and the CME guidance. At the same time, the Agency recognizes that a manufacturer may have a First Amendment defense in a "misbranding" action based on non-
compliance with these requirements. 102

Under these circumstances, even though the agency's concession is an apparent victory for WLF, the organization remains circumspect about FDA's intent to comply with the spirit of Judge Lamberth's decisions. WLF Chief Counsel Richard Samp indicated that "[w]e will be keeping a close eye on FDA; the very first time FDA so much as suggests that manufacturers could be sanctioned for distributing truthful information of the type covered by the injunction, we will be back in district court seeking to have FDA held in contempt." 103

The Agency has now made the first such suggestion, reiterating its position in the Federal Register of March 16, 2000 that the FDAMA and the CME guidance establish a "safe harbor" for manufacturers who comply with them, but insisting that it may still use a manufacturer's non-compliance as evidence of a medical product's true "intended use" in an action for misbranding. 104 WLF disagrees with this interpretation and reportedly intends to make a motion to enforce Judge Lamberth's earlier order, which in WLF's view still bars the agency from prohibiting the dissemination of information on off-label uses. Clearly, the fight isn't over; quite possibly it has just begun.

V. INDUSTRY GIFTS TO PHYSICIANS: SUPPORTING INNOVATION OR "BUYING SCIENCE"?

As medical device and pharmaceutical manufacturers have intensified their marketing efforts, they have developed new ways to broaden their relationships with doctors. The orthopedic bone screw litigation of the late 1990's illustrates the perils of these marketing strategies if the product later becomes the subject of litigation.

The bone screw litigation involved more than 2,000 civil actions from all over the country that were consolidated for pre-trial purposes in the U.S. District Court for the Eastern District of Pennsylvania. 105 The plaintiffs claimed to have suffered injuries from allegedly defective rods, plates, and screws placed in their spine in

102. 65 FR 14287 (March 16, 2000).
104. 65 FR 14287 (March 16, 2000).
order to alleviate their severe back conditions. But more than a year after the first complaints were filed, the plaintiffs expanded their claims beyond the well-worn products liability theories typically found in medical mass torts. In these "Omni" actions, the plaintiffs alleged that the manufacturers, certain medical professional associations, and individual doctors conspired to hoodwink the FDA and defraud hundreds of orthopedic surgeons who would not have implanted the devices into the plaintiffs had they known the real risks of the procedure. The allegations amounted to a claim that the device industry and the medical profession had conspired to "buy the science" that would support ongoing sales of bone screw devices.

The alleged conspiracy was based on agreements between the manufacturers, the medical associations, and the doctors that the doctors would make presentations on spinal fixation of the device—an unapproved, "off-label" use—in exchange for royalties relating to sales of the product and for shares in the manufacturers' companies. According to the complaints, although the seminars did not on the surface appear different from other CME programs, they really amounted to "Tupperware parties" since their purpose was purely commercial. The doctors did not disclose to seminar attendees that the procedure they were demonstrating was "off-label" and not approved by the FDA, nor did they disclose their direct financial interest in the success of the product and the company that made it.

While the "Omni" conspiracy claims were dismissed with prejudice, they nevertheless are significant as a first salvo fired into uncharted territory. The manufacturers, medical associations, and doctors named in the suits spent millions fending them off. The suits also exposed the extent to which industry promotional practices pervade continuing medical education events, a revelation that is troubling to many. While the plaintiffs' bar lost this time, they no doubt learned valuable lessons in the bone screw litigation—lessons that could reverse their fortune the next time around.

106. Id.
107. Id. at 786.
108. Id.
109. Id.
110. Id. at 786-77.
111. Id. at 792.
A. Influence In Practice: The JAMA Study On Physician Gifts And Prescribing Practices

One piece of evidence that future conspiracy plaintiffs will likely use is a January, 2000 study published in the *Journal of the American Medical Association* on the influence of gifts on physicians' prescribing practices.\(^{112}\) The study, a compilation of data from 538 other studies on the subject, resulted in the following startling conclusions:

Meetings with pharmaceutical representatives were associated with requests by physicians for adding the drugs to the hospital formulary and changes in prescribing practice.

Drug company-sponsored continuing medical education (CME) preferentially highlighted the sponsor's drug(s) compared with other CME programs.

Attending sponsored CME events and accepting funding for travel or lodging for educational symposia were associated with increased prescription rates of the sponsor's medication.

Attending presentations given by pharmaceutical representative speakers was also associated with non-rational prescribing.\(^{113}\)

In Commentary published in the same issue as the study, Dr. Robert M. Tenery notes that many doctors are not even aware of the extent of influence that industry-sponsored activities and gifts have on their prescribing practices.\(^{114}\) He advocates that:

Even though it may be desirable to encourage information sharing, relationships between physicians and industry raise concerns about whether the patient's best interests will come into conflict with industry's focus on the bottom line. Physicians should not take as absolute everything they are told by industry representatives and should become cognizant of the potential conflicts created by the increasing level of sophistication in the detailing techniques used by these individuals.\(^{115}\)

---


\(^{113}\) Id. at 375-377.


\(^{115}\) Id.
B. Expanding The Sphere Of Influence: "Detailing" To Nurse Practitioners And Physicians' Assistants

Today, manufacturers' promotional efforts extend well beyond physicians, as seen in the discussion of direct-to-consumer advertising. But even within the medical community, doctors are no longer the exclusive focus of drug marketers. As Nurse Practitioners (NP) and Physicians' Assistants (PA) receive ever-greater prescribing authority, pharmaceutical and medical device "detailers" are targeting them with more and more promotional efforts. Some physicians find this a cause for concern.

While non-physician prescribers, like doctors, insist that company representatives are only one source of their information on medical products, they are nonetheless subject to a barrage of sales pitches. A survey by Scott-Levin Associates revealed that PAs averaged 4.4 visits per week from detailers, and NPs averaged 5.2. These visits are only expected to increase.

In addition to the frequency of the visits, there is a concern that nurse practitioners and doctors' assistants are particularly susceptible to "hard sell" efforts by medical products retailers. One commentator claims that such "physician extenders" do not have "the knowledge base to understand pharmacology and the complexities of medicine." He quips that "[t]hey are given samples of advanced antibiotics, invited out to dinner and are being prepped to use these samples." Fearing that "drug companies are simply looking for the weakest link in the practice," he postulates that nurse practitioners and physician assistants are being targeted because they are "most likely to comply with marketing and sales messages."

Whether non-physician prescribers are this easily swayed by detailers can be argued, but there is no disputing the fundamental shift in the demographics of medical products sales. As marketing to non-physicians escalates, doctors are less available to company salespeople than ever before. In addition, as consumers receive

117. Id.
118. Id.
119. Id.
120. Id.
121. Id.
more advertising messages about new products, they specifically request certain name-brand medications, and primary care physicians, given their time constraints, are increasingly delegating such requests to their assistants.\footnote{123}

Further, according to the Scott-Levin survey, 80\% of PAs and 69\% of NPs recommend new drugs to the doctors with whom they work,\footnote{124} which may influence the extent to which these products are ultimately prescribed. At the same time, Dr. Yank Coble of the American Medical Association expressed that "I don't get my information on new drugs from nurses, and I don't think many other doctors do either."\footnote{125} Thus, it remains unclear just how much stepped-up marketing to non-physicians has actually influenced prescribing practices.

It is also worth noting, however, that the increase in non-physician prescribing, along with the intensified sales efforts directed at PAs and NPs, could have dire consequences for the learned intermediary doctrine. If it is indeed "unrealistic," as Dr. Coble claims, "to suddenly expect people with less training than doctors to interpret research for patients,"\footnote{126} then courts will have no choice but to ignore the learned intermediary doctrine and require manufacturers to provide warnings directly to consumers.

VI. REPROCESSING AND REUSE OF SINGLE USE DEVICES

With the increased cost-control pressures of managed care, along with the ascendance of for-profit hospitals, providers today have every incentive to cut costs wherever they can. Thus, many providers have begun cleaning ("reprocessing") and returning to circulation so-called "single-use" medical devices. Hospitals and medical centers can save tens of thousands of dollars per year by reusing such devices.\footnote{127} Further, doctors argue that the prices manufacturers charge are so prohibitive that they cannot afford to use a device just once, and costs cannot be passed along to patients because the rates are usually set by insurance companies or medi-

\footnote{123. \textit{Id}.} \footnote{124. \textit{Id}.} \footnote{125. \textit{Id}.} \footnote{126. \textit{Id}.} \footnote{127. Gina Kolata, "Single Use" Medical Devices Are Often Used Several Times, \textit{N.Y. Times}, November 10, 1999.}
Dr. David Haines of the University of Virginia Health System claims that if they were forced to use cardiac catheters only once, as the manufacturer's labeling directs, "we would shift from being marginally profitable to probably losing $600,000 a year." Many also point to the fact that some devices initially labeled "reusable" were switched to "single-use" without any structural changes, making it appear that the switch had more to do with marketing than safety. 129

While Dr. Larry Kessler, director of the office of surveillance and biometrics at FDA, acknowledges that "there's a big yuck factor to reusing devices," he maintains that nevertheless "there are no products where we have significant evidence that there is immediate harm to public health." 130 Published studies by Dr. Richard A. Kozarek, chief of gastroenterology at Virginia Mason Medical Center in Seattle, show that various devices can safely be reused numerous times, generating a substantial savings for health-care providers. 131 Further, of the more than 100,000 yearly adverse reports concerning devices, virtually all involve devices used just once. 132 Of course, as Dr. Kessler acknowledges, if a reprocessed device failed, "[d]o you think the hospital would want to tell anyone? They are worried that they will be in court and in serious trouble." 133

So far, FDA has refrained from requiring reprocessors of single-use devices to prove that the products are "safe and effective" when they leave their hands, but this may change as medical device manufacturers are increasingly challenging the practice. 134 Despite charges that the industry's complaints are motivated by their profit margins, medical device manufacturers argue that the real issue is patient safety. 135 Patricia Davis, an electrical engineer and senior patent attorney at Boston Scientific, a leading manufacturer of coronary stents, claims that studies by her company indicate that devices are often contaminated and degraded when they leave the

---

128. Id.
131. Id.
132. Id.
133. Id.
134. Id.
135. Id.
reprocessor. She warns that subtle changes in a device's functioning upon reuse can have devastating consequences for patients. Another commentator raises the concern that since single-use devices are not made to be cleaned and reused, "the very design structure did not take into account the need to access all the nooks and crannies in order to clean them." This increases the risk of infection, which he claims patients should be informed of.

Robert O'Halla, Vice President of Regulatory Affairs for Medical Devices and Diagnostics at Johnson & Johnson and Chairman of the Association of Disposable Device Manufacturers, argues that there is no reason to treat reprocessors differently than original equipment manufacturers (OEMs). OEMs are required to obtain either 510(k) clearance or pre-market approval for their single-use devices. When they are approved, they are approved for one use only, since no data supports their safety and efficacy beyond that. Therefore, when a reprocessor prepares a device for reuse, as a regulatory matter this is tantamount to creating a new device. Yet to this point, FDA has exercised its "regulatory discretion" to not require reprocessors to submit 510(k) or pre-market approval applications—even while recognizing that the same provisions of the Food, Drug & Cosmetic act that apply to OEMs also apply to reprocessors.

Under increased pressure from manufacturers, and recognizing the inconsistency of their position, FDA is in the process of formulating regulations for reprocessing of single-use devices. In testimony before Congress, Dr. David Feigal, Director of FDA's Center for Devices and Radiological Health (CDRH), indicated that the Agency plans "a new regulatory approach that will treat
Original Equipment Manufacturers...third parties and hospitals in a similar manner to minimize risks associated with reused single-use devices.\textsuperscript{144} For now, FDA is receiving comments on its February 8, 2000 draft Guidance which presents a "Review Prioritization Scheme" for assessing the safety of reprocessing different categories of devices.\textsuperscript{145} Through a series of flow charts, devices will be characterized as low, medium, and high risk for reprocessing based on answers to questions like:

Does postmarket information suggest that using the reprocessed SUD [(single-use device)] may present an increased risk of infection when compared to the use of a SUD that has not been reprocessed?

Does the SUD include features that could impede thorough cleaning and adequate sterilization/disinfection?\textsuperscript{146}

Other countries are also evaluating the use of single-use devices. Canada is conducting a review of the practice after the province of Manitoba instituted a ban on hospital reprocessing.\textsuperscript{147} Belgium is considering a ban on reuse of angioplasty balloons, electrophysiology catheters, biopsy forceps and other delicate devices used in invasive procedures.\textsuperscript{148} In the United Kingdom, the Medical Device Agency has taken a stance against reuse due to a concern with the transmission of Creutzfeld-Jakob or "mad cow" disease.\textsuperscript{149}

Of course, while reproprocessors face liability for contaminated devices that leave their cleaning facilities, manufacturers may ultimately bear more of the burden for injuries resulting from failures of reprocessed devices. When reports of injuries from reused devices started to accumulate, instead of questioning reproprocessors on the adequacy of their procedures, FDA suggested that OEMs should compile data on risks associated with reprocessing and reuse.\textsuperscript{150} In addition, since manufacturers will often more capitalized

\textsuperscript{146.} \textit{Id.}
\textsuperscript{148.} \textit{Id.}
\textsuperscript{149.} \textit{Id.}
than reprocessing operations, they will inevitably be a target in litigation stemming from such injuries. Finally, manufacturers could be found negligent for not guarding against "foreseeable misuse" by providing instructions for proper cleaning, and for not making devices sturdy enough for reuse—notwithstanding the "single use only" warning—because they will usually have actual or constructive knowledge that purchasers are reusing their products. Whether the medical manufacturing industry can reduce this exposure by pressuring FDA to adopt "pre-market approval" regulations, requiring reprocessors to prove the safety and efficacy of reused devices, remains to be seen.

VII. CONCLUSION

The future of drug and medical device litigation promises to be as contentious as the past, although the issues have changed. Where the last 50 years saw the growth of the law with respect to the healthcare product, in the future—as this discussion has shown—new developments in the law will come more from the relationships surrounding the product: between industry and the consumer, between physician and industry, between industry and the FDA, and even between rival healthcare industries. What will remain unchanged, however, is the intensity of the conflict as the law struggles to reconcile itself with the new realities of medical technology in the 21st Century.