Informed Consent: Requiring Doctors to Disclose Off-Label Prescriptions and Conflicts of Interest

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INTRODUCTION

Your doctor just prescribed a new drug to ease your back pain. Wouldn’t you want to know that: (1) the Food and Drug Administration (FDA) approved the drug for epilepsy, not back pain; (2) no reliable research supports using the drug for back pain; (3) your doctor learned about using the drug to treat back pain while vacationing on Maui at the drug manufacturer’s expense; and (4) the drug company is paying your doctor to prescribe this drug? While this scenario is surprisingly common,1 the current doctrine of informed consent does not require your doctor to disclose these facts.2 This Article will explain why it should.3

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1. See infra Part I.A discussing off-label prescribing; Part I.B.2 discussing the lack of reliable research for off-label uses; Part I.B.3 discussing drug company sponsorship of continuing medical education; Part I.B.2 discussing Phase IV surveillance studies.

2. See infra Part II.B explaining that the doctrine of informed consent law does not require these disclosures; see also James M. Beck & Elizabeth D. Azari, FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions, 53 FOOD & DRUG L.J. 71, 91 (1998) (“[N]o appellate cases have held that a physician’s failure to disclose that a drug therapy was prescribed off-label violated informed consent.”) (quoting William L. Christopher, Off-Label Drug Prescription Filling the Regulatory Vacuum, 48 FOOD & DRUG L.J. 247, 255 (1993))); Steven R. Salbu, Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy, 51 FLA. L. REV. 181, 190, 223 (1999); Bernadette Tansey, Off-Label Disclosure on Drugs Proposed, S.F. CHRON, Feb. 25, 2006, at C1 (reporting that the author of a proposed California statute requiring disclosure of off-label uses knew of no state, including California, requiring disclosure that a
A majority of patients believe that doctors always prescribe drugs as approved by the FDA. According to a poll published by the Wall Street Journal Online, "There is a massive public ignorance of 'off-label prescribing,' the widespread practice of prescribing drugs to treat diseases where the FDA has not approved this use of the drug." In fact, doctors frequently prescribe drugs for treatments which are not FDA approved. Indeed, the American Medical Association (AMA) estimated that 40% to 60% of prescriptions are for unapproved uses. These prescriptions are referred to as "off-label" because they do not conform to the FDA-approved use set out in the FDA-approved label. An off-label prescription may depart from the FDA label if the drug is prescribed for a different purpose, for a different patient group, for a longer duration, or in a combination which has not been approved by the FDA.

Off-label prescribing is a common, important, and necessary practice. For example, pediatric prescriptions are frequently off-label because many drugs are not tested for treating children. Aspirin was widely prescribed to reduce the risk of heart attack long before it was FDA-approved for this purpose. Off-label uses have proven effective in treating cancer patients. And off-label, antiretroviral combination therapies have prolonged the lives of thousands of AIDS patients. In short, off-label prescribing is a significant part of mainstream medicine. As an officer of the AMA explained, "[I]n some cases, if you didn’t use treatment is off-label).
the drug in the off-label way you'd be guilty of malpractice."

While off-label prescriptions are common and often necessary, they present substantial risks. In many off-label uses, the drug or device has not been proven safe or effective for treating the patient's condition. In fact, a 2006 study published in the *Archives of Internal Medicine* found that most off-label prescribing "occurs without scientific support." In some instances, FDA panels have investigated off-label uses and found them to be ineffective or dangerous. For example, doctors wrote eighteen million prescriptions for the off-label use of Fenfluramine for weight loss before it was discovered that nearly three hundred thousand people suffered heart valve damage from it. Unfortunately, this is not an isolated instance where off-label uses created substantial health risks. A recent example is Letrozole. The FDA approved Letrozole as a breast-cancer therapy for post-menopausal women, but required a warning that it was known to be associated with birth defects. Despite this warning, in 2005 a number of fertility doctors prescribed the drug off-label to help women become pregnant.

The most recent example is Actimmune, which has been prescribed off-label to patients with a potentially fatal lung condition, idiopathic pulmonary fibrosis. Actimmune is approved by the FDA to treat two other extremely rare diseases, but substantially all its sales—about $90 million in 2006—are from the off-label use for pulmonary fibrosis, which costs each patient about $50,000 per year. There is no reliable evidence that Actimmune is an effective treatment for pulmonary fibrosis. In March 2007, InterMune abandoned its efforts to develop Actimmune as


17. Radley et al., supra note 10, at 1021.

18. Salbu, supra note 2, at 211; Stoffelmayr, supra note 15, at 280.


21. Cancer Drug No Fertility Treatment, supra note 20; see infra note 88 (providing additional examples).


23. Id.

24. See id.
a treatment for pulmonary fibrosis because clinical trials showed that it failed to prolong lives and was no more effective than a placebo.\textsuperscript{25}

Off-label prescribing is often appropriate, but it requires careful consideration of the benefits and risks. It’s one thing to prescribe a drug off-label for a serious condition when there is no FDA-approved therapy, especially when reliable research supports the off-label use. It’s another to prescribe a drug off-label where there is a safe and effective FDA-approved alternative or where the patient’s condition is not sufficiently serious to warrant the risks of an unproven and potentially dangerous treatment.

The frequency of off-label prescribing has increased substantially over the past few years.\textsuperscript{26} Prescription drugs are a huge and highly profitable business.\textsuperscript{27} The drug companies increase sales by expanding their market to off-label uses.\textsuperscript{28} While the FDA previously restricted the industry’s off-label marketing, the regulatory restrictions were challenged on First Amendment grounds.\textsuperscript{29} In many cases, the off-label uses are not based on reliable scientific research.\textsuperscript{30} As this Article explains, off-label prescribing drives up the cost of medical care and exposes patients to unnecessary health risks.

Additionally, patients are unaware of industry marketing practices that create conflicts of interest for doctors.\textsuperscript{31} Drug companies sponsor and publish shoddy research and present it to doctors at free educational programs, often hosted at fashionable resorts with complimentary gourmet meals and rounds of golf.\textsuperscript{32} They pay doctors to attend and to present the marketing programs.\textsuperscript{33} They also pay doctors to prescribe their drugs under the guise of “research” which is scientifically worthless.\textsuperscript{34} They shower doctors with gifts and free samples to encourage prescribing.\textsuperscript{35} The strategy works. According to studies reported in the \textit{Journal of the American Medical Association}, in response to drug company promotions doctors prescribe drugs more frequently and nonrationally.\textsuperscript{36}

\textsuperscript{25} Id.
\textsuperscript{26} Moyer, \textit{supra} note 6, at 931.
\textsuperscript{27} \textit{See infra} notes 40–52 and accompanying text.
\textsuperscript{28} \textit{See discussion infra} Part I.A; \textit{see also} Angell, \textit{supra} note 7, at 156–57; O’Reilly & Dalal, \textit{supra} note 16, at 299–300; Stoffelmayr, \textit{supra} note 15, at 279.
\textsuperscript{29} Wash. Legal Found. v. Henney, 56 F. Supp. 2d 81 (D.D.C. 1999); \textit{see infra} notes 151–55 and accompanying text.
\textsuperscript{30} \textit{See discussion infra} Part I.B.1.
\textsuperscript{31} \textit{See Tansey, supra} note 4; \textit{Harris Poll, supra} note 4.
\textsuperscript{32} \textit{See discussion infra} Parts I.B.2–3.
\textsuperscript{33} \textit{See discussion infra} Part I.B.4.
\textsuperscript{34} \textit{See infra} notes 189–96 and accompanying text.
\textsuperscript{35} \textit{See discussion infra} Part I.B.6.
\textsuperscript{36} Ashley Wazana, \textit{Physicians and the Pharmaceutical Industry: Is a Gift Ever Just a Gift?}, 283
This Article proposes that the tort doctrine of informed consent should be expanded to require doctors to disclose off-label prescriptions and conflicts of interest. It begins by describing current practices in off-label prescribing, pharmaceutical marketing, and their regulation. Specifically, Part I.A outlines the widespread and entirely legal practice of off-label prescribing. Part I.B covers drug-company marketing practices and the conflicts of interest they create for doctors. Part II analyzes the doctrine of informed consent and explains why it should be expanded to require disclosure of off-label prescriptions and conflicts of interest. Finally, Part III presents the disclosures contemplated by the proposed expansion of the doctrine of informed consent.


37. See infra Part III.B. Other scholars have suggested reforms to address these problems. See Mitchell Oates, Facilitating Informed Medical Treatment Through Production and Disclosure of Research into Off-Label Uses of Pharmaceuticals, 80 N.Y.U. L. REV. 1272 (2005); Radley et al., supra note 10, at 1025–26 (proposing policy-makers develop mandatory programs for more extensive post-marketing surveillance to identify non-evidence-based prescribing practices that lacked FDA approval); Salbu, supra note 2, at 217–27 (proposing several reforms including patient disclosure of off-label uses); Jaime A. Wilsker, One-Half Phen in the Morning/One Fen Before Dinner: A Proposal for FDA Regulation of Off-Label Uses of Drugs, 8 J.L. & POL’Y 795, 839 (1998); David M. Fritch, Comment, Speak No Evil, Hear No Evil, Harm the Patient? Why the FDA Needs to Seek More, Rather than Less, Speech from Drug Manufacturers on Off-Label Drug Treatments, J. MED. & L. 315, 365-67 (2005) (proposing that the FDA should require disclosure of all clinical trial information). While these proposals are all promising, in my view they are not likely to be adopted by Congress, the FDA, or state legislatures, at least at this time. I am not the first to conclude that “tort law, however imperfect, may be the only mechanism for assuring that patients get the information they need to weigh their physicians’ recommendations, especially when those recommendations may be tainted by a financial conflict of interest.” Grant H. Morris, Dissing Disclosure: Just What the Doctor Ordered, 44 ARIZ. L. REV. 313, 369 (2002) (citing Barry R. Furrow, Managed Care Organizations and Patient Injury: Rethinking Liability, 31 GA. L. REV. 419, 509 (1997); Deven C. McGraw, Financial Incentives to Limit Services: Should Physicians be Required to Disclose These to Patients, 83 GEOR. L.J. 1821, 1844 (1995)).

Currently, the FDA lacks the resources to monitor drugs and their promotion after initial approval. See Oates, supra, at 1300 (discussing the insufficient resources at the FDA to monitor post-approval uses since the primary focus of the agency is new drug approval); see also Jonathon D. Rockoff, FDA Scientists Blast Agency’s Priorities, S.F. CHRON., July 21, 2006, at A6 (reporting on a survey by the Union of Concerned Scientists finding that 70% of responding FDA scientists believed that the agency lacked the resources required to carry out its mission and 81% said the agency needed to strengthen its oversight of drugs after they go on sale). Moreover, armies of drug company lobbyists frustrate proposals for marketing restraints. According to one report, the industry has 1274 lobbyists in Washington—more than two for each and every member of Congress. Jim Drinkard, Drugmakers Go Furthest to Sway Congress, USA TODAY, Apr. 16, 2005, at B1. In 2004, the industry spent $158 million to lobby the federal government, $17 million in campaign contributions to federal candidates, and $7.3 million to support political party conventions. Id.; see also KATHARINE GREIDER, THE BIG FIX 144 (2003). Indeed, when Congress attempted to regulate marketing by adopting the balanced provisions of the FDAMA, the industry successfully challenged the restrictions on First Amendment grounds. See infra notes 151–55 and accompanying text. Finally, the industry lobby is equally active on the state level. Specifically, from 2001 to 2004, drug company executives, employees, and political action committees donated more than $18 million to state political groups and candidates and a whopping $83 million to lobby on the California health care and drug discount referendum in 2005. M. Asif Ismail, Deep Pockets Contribute to Success, CYR. FOR PUB. INTEGRITY, Apr. 6, 2006, http://www.publicintegrity.org/rsx/report.aspx?aid=795.
I. OFF-LABEL PRESCRIPTIONS, PHARMACEUTICAL MARKETING, AND THEIR REGULATION

This Part will describe two aspects of health care in the United States today: (A) off-label prescribing; and (B) pharmaceutical marketing. Off-label prescribing, as briefly explained above, is a significant part of current medical practice. It allows patients to receive needed treatments before the lengthy regulatory process has been completed. And, since the FDA does not regulate the practice of medicine, off-label prescribing is not subject to FDA restrictions. As a result, roughly half of the prescriptions written today are for uses outside the scope of FDA approval. Pharmaceutical marketing is a multi-billion dollar industry aimed at influencing doctors’ prescribing decisions. As recently reported in the *Journal of the American Medical Association*, pharmaceutical marketing practices create conflicts of interests for prescribing doctors.

A. OFF-LABEL PRESCRIBING AND ITS REGULATION

Prescription drugs are big business. The United States pays virtually the highest prices for prescription drugs of any country in the world. Prescription drugs are the fastest growing part of health care costs with spending increasing at double-digit rates for each year from 1997 to 2005. Between 1990 and 2002, the amount spent on prescription drugs in the United States increased fourfold from $40.6 billion to $162 billion. From 1993 to 2003, prescription drug prices increased 7.4%, while inflation increased 2.5%. Most recently, prescription drug sales rose from $238.9 billion in 2004 to $251.8 billion in 2005. National spending on prescription drugs is projected to grow at an annual rate of 10.7% from 2004 to 2013. That estimate may, in fact, be low. A recent report found that brand-name drug prices rose nearly 4% during the first year.

38. Angell, supra note 7, at 204.
40. Greider, supra note 37, at 17.
42. Nat’l Ass’n of Attorneys Gen., supra note 41, at 7; see also Kapp, supra note 41, at 237 (stating that drug spending has been increasing at an annual rate of 18%).
44. Id. at 16.
45. Duncan Moore, Prescription Drug Sales Rise 5.4% for 2005, S.F. Chron., Feb. 23, 2006, at C3; see also Angell, supra note 7, at 3-4.
three months of 2006.\textsuperscript{47} Prices for the 200 top-selling drugs are rising at three times the rate of inflation.\textsuperscript{48} The drug industry is tremendously profitable—usually the most profitable industry in the country.\textsuperscript{49} In 2002, profits were 17\% of sales\textsuperscript{50} while the median profits for all Fortune 500 companies were only 3.1\% of sales.\textsuperscript{51} To put this figure in perspective, the profits of the ten drug companies on the Fortune 500 list in 2002 were greater than the combined profits for the other 490 businesses.\textsuperscript{52}

Since the New Deal, the FDA has regulated the drug industry under the 1938 Food, Drug, and Cosmetics Act ("FDCA").\textsuperscript{53} In response to deaths from the presence of a poisonous solvent in sulfa drugs, Congress created the FDA and mandated that it regulate the safety of drugs.\textsuperscript{44} In 1962, horrified by the thousands of babies severely deformed by the drug thalidomide, Congress adopted the Kefauver-Harris Amendments which expanded FDA authority to assure the effectiveness of drugs before they could be sold in the United States.\textsuperscript{55} Under these amendments, the FDA has absolute authority to examine the scientific evidence of safety and efficacy of drugs.\textsuperscript{56} In this statutory scheme, the FDA’s approval of a new drug must be based on extensive scientific evidence establishing that it is safe and effective.\textsuperscript{57}

The FDA approval process takes six to fifteen years\textsuperscript{58} and costs between $100 million and $880 million per drug.\textsuperscript{59} The process first
requires animal testing. After this phase, the manufacturer files an application with the FDA as an Investigative New Drug (IND) to begin clinical trials on humans. Three phases of human testing are required: preliminary testing (Phase I); testing a small target population (Phase II); and large-scale, double-blind testing (Phase III). During all three phases, FDA regulations require researchers to obtain the informed, written consent of patients. Once the required testing is completed, the manufacturer submits a New Drug Application (NDA) to the FDA which must report on all stages of testing. In the past twenty years, the time required to obtain FDA approval of an NDA has dropped from about twenty-two months to about twelve months for most drugs and less than six months for drugs that treat life-threatening conditions.

While the FDA requires the applicant to show the drug is safe and effective, the applicant does not have to show the drug works better than existing drugs. The applicant need only show that the new drug works better than a placebo. In other words, the applicant must show the new drug is better than nothing at all. Given this low regulatory standard, "we usually have no idea whether a new drug is any better than an old one." Often the "new" drugs are not truly innovative but are "me-too" drugs—minor variations of drugs already on the market. For example, in 2002, the FDA approved seventy-eight drugs, but "only seventeen contained new active ingredients and only seven of these were classified by the FDA as improvements over older drugs."

Moreover, FDA approval does not mean that the product poses no risks because the FDA cannot possibly identify every potential risk before approval. The FDA acknowledges that some risks will not be discovered until after the drug is approved and widely used. This reflects the inherent tension between the competing goals of getting

60. NAMJOSHI, supra note 55, at 9.
63. Beck & Azari, supra note 2, at 75, 86.
64. 21 C.F.R. § 314 (2006); Beck & Azari, supra note 2, at 75–76.
65. NAMJOSHI, supra note 55, at 9. Critics question how reliable this research is since increasingly the drug companies run the clinical trials. ANGELL, supra note 7, at 28–29, 99–103.

67. Id. at 18, 23.
68. Id. at 23.
69. ANGELL, supra note 7, at 74–93; Angell, supra note 41, at 67.
70. ANGELL, supra note 7, at 16–17.
71. Id.
72. Henney, supra note 66.
73. Id.
effective new treatments to patients as soon as possible and extensively testing new drugs to ensure patient safety. Thus, even drugs approved as safe and effective have turned out to have undetected risks that have endangered patients. The recent withdrawal of the drug Vioxx from the market illustrates the point.\textsuperscript{74} For this reason, it is usually safer for patients to take an older drug with an established track record than a newer drug even if it has been FDA-approved for the condition being treated.\textsuperscript{75}

Unfortunately, the FDA lacks the authority and resources required to monitor the safety of drugs after they have been approved. A recent federal investigation concluded that the FDA lacked sufficient authority to require drug companies to conduct studies of prescription medicines already on the market.\textsuperscript{76} The 2006 report by the Government Accountability Office (GAO) found that the FDA lacked an effective process for oversight of post-approval drug safety.\textsuperscript{77} Even where the FDA required post-approval studies—often as a condition of granting expedited approval—the FDA itself reported that nearly two-thirds of the 1231 studies that drug companies had promised to conduct had yet to be initiated.\textsuperscript{78} Senator Charles Grassley, who requested the GAO investigation, has co-sponsored legislation to establish an independent center for post-approval monitoring.\textsuperscript{79} Indeed, there is broad agreement in Congress and among experts that better post-approval monitoring is necessary.\textsuperscript{80}

While the FDA fails to effectively monitor post-approval safety, it does regulate the information, which must accompany the drug in the Patient Package Insert (PPI).\textsuperscript{81} This package insert is restricted to information about approved uses,\textsuperscript{82} which is compiled and published in the Physicians' Desk Reference (PDR).\textsuperscript{83} Moreover, "[n]o implied claims or suggestions of drug use may be made if there is inadequate evidence


\textsuperscript{75} GREIDER, supra note 37, at 98.

\textsuperscript{76} Andrew Bridges, Probe Finds FDA Needs More Muscle, S.F. CHRON., Apr. 24, 2006, at A2.

\textsuperscript{77} Alison Torres Burtka, GAO Report Criticizes Drug Safety Oversight, TRIAL, July 2006, at 22.

\textsuperscript{78} Bridges, supra note 76, at A2.

\textsuperscript{79} Burtka, supra note 77, at 92.

\textsuperscript{80} Okie, supra note 66, at 1063.

\textsuperscript{81} Kapp, supra note 41, at 238; Salbu, supra note 2, at 187.

\textsuperscript{82} Moyer, supra note 6, at 930; Salbu, supra note 2, at 187.

\textsuperscript{83} Kapp, supra note 41, at 238; Salbu, supra note 2, at 187.
of safety or... effectiveness.\textsuperscript{84}

After a drug is approved, researchers and doctors often discover new applications for it.\textsuperscript{85} Once a drug is FDA-approved for a single specific use, doctors may prescribe it to \textit{any} patient for \textit{any} use and are not restricted to prescriptions that comply with the FDA approval.\textsuperscript{86} The FDA considers these treatments "off-label" because substantial evidence regarding their safety and efficacy has not been presented or evaluated.\textsuperscript{87} But such uses are perfectly legal. In fact, FDA policy explicitly states that "once a [pharmaceutical] product has been approved for marketing, a physician may prescribe it for uses in treatment regimes of patient populations that are not included in the approved labeling."\textsuperscript{88} Indeed, as the Supreme Court has recognized, off-label prescribing "is an accepted and necessary corollary of the FDA's mission to regulate in this area without directly interfering with the practice of medicine."\textsuperscript{89} Simply put, the FDCA was not intended to regulate the practice of medicine.\textsuperscript{90} In other words, the FDA does not regulate off-label drug prescribing even though it is a key component in medical practice today.

As explained in the PDR, the FDA has also recognized that the FDCA does not, however, limit the manner in which a physician may use an approved drug. Once a product has been approved for marketing, a physician may choose to prescribe it for uses in treatment regimens or patient populations not included in approved labeling. The FDA also observes that accepted medical practice includes drug use that is not reflected in approved drug labeling.\textsuperscript{91}

In addition to being accepted medical practice, off-label prescribing often provides optimal patient care.\textsuperscript{92} For example, for many years aspirin was prescribed to reduce the risk of heart attack but was not approved for this use until 1998.\textsuperscript{93} Off-label uses that represent a logical extension of the original FDA-approved use are often seen as clinically acceptable treatments.\textsuperscript{94} Moreover, off-label uses are frequently the only available treatment for some serious and fatal diseases. Specifically, 62%
of cancer patients use drugs off-label. Indeed, off-label uses in some cases represent the highest standard of care, especially in treating AIDS, cancer, and rare diseases.

But, as explained above, not all off-label uses are safe. Indeed, some off-label uses are "costly, threatening, and highly toxic." For example, the widely-prescribed diet drug, Fenfluramine, was never approved for long-term use and, in fact, caused heart valve damage to at least 285,000 patients, according to the FDA. Oxycontin, a dangerously addictive, morphine-based drug, was promoted for general pain relief. While it is an extremely valuable drug for the treatment of severe pain, it was overprescribed and abused, becoming the most frequently prescribed pain medication in the country, and leading to hundreds of unnecessary deaths. Today, the highly addictive pain treatment Actiq, which is FDA-approved for intense cancer pain that is unresponsive to other drugs, is frequently prescribed for non-cancer patients suffering headaches and back pain. Indeed, research suggests that 80% of the

95. NAMJOSHI, supra note 55, at 2.
97. Salbu, supra note 2, at 202 (quoting Maryann Napoli, Chemotherapy and Informed Consent, HEALTHFACTS, Sept. 1997, at 1, 5) (internal quotation marks omitted). For example, Zyprexa, Risperdal and other atypical antipsychotics are prescribed off-label to treat dementia. According to the FDA, "[W]hen prescribed off label as a treatment for dementia, older patients had a higher chance for death than patients who did not take the medicine." Alison Young, FDA Launches Site to Warn Patients, Doctors of Drug Risks, KNIGHT RIDDER TRIB. NEWS SERVICE, May 20, 2005, at 1, http://www.yourlawyer.com/articles/read/9749; see also U.S. Food & Drug Admin., FDA's New Drug Safety Initiative, http://www.fda.gov/cder/drugSafety.htm (last visited Mar. 29, 2007). Amiodarone (also marketed as Cordarone and Pacerone) is approved to treat a specific, life-threatening heart rhythm disorder but is frequently prescribed off label for non-life-threatening atrial fibrillation. Id. According to the FDA, the drug has potentially fatal side effects including lung toxicity, liver injury, and worsened heart rhythm problems. Id. Gabitril, a drug approved to treat seizures, is most frequently prescribed for psychiatric conditions including bipolar disorder. Id. According to the FDA, the drug has only been approved for treating seizures and its "safety and effectiveness have not been established for any other use." Id. Even its manufacturer, Cephalon, has initiated efforts "to discourage off-label use." Id. As its spokesperson explained, it has not done sufficient studies to support the off-label use and the "scientific team doesn't believe there is sufficient evidence that a drug like Gabitril would be effective in bipolar disorder." Id. Indeed, "when used off-label, the drug has been associated with seizures in people without epilepsy." Id.
98. NAMJOSHI, supra note 55, at 2; O'Reilly & Dalal, supra note 16, at 300; Salbu, supra note 2, at 203; Paul D. Rheingold & David B. Rheingold, Offense or Defense? Managing the Off-Label Use Claim, TRIAL, Mar. 2001, at 52; see also Hershel Jick et al., A Population-Based Study of Appetite-Suppressant Drugs and the Risk of Cardiac-Valve Regurgitation, 339 NEW ENG. J. MED. 719 (1998) (finding that the use of fenfluramine for four months or longer is associated with an increased risk of cardiac-valve damage); Sachdev et al., supra note 19, at 1071 (estimating that in 1996 alone, 18 million fenfluramine prescriptions treated 1.5 million patients, leading to 30,500 fenfluramine-related cases of cardiac-valve damage).
patients who use the drug do not have cancer. Recently, a breast cancer drug was increasingly prescribed off-label as a fertility treatment despite its reported association with birth defects. An ulcer drug is used off-label in labor and delivery cases despite the risk of a ruptured uterus. The list of examples is numerous and frightening.

A 2006 study published by the AMA underscores the risks of off-label prescribing. It found that off-label prescribing is common and usually lacks scientific support. Specifically, 73% of the off-label uses studied “lacked evidence of clinical efficacy, and less than one-third (27%) were supported by strong scientific evidence.” It cautioned that under-evaluated off-label practices—those not supported by strong scientific evidence—may “jeopardize patient safety or represent economically wasteful prescribing practices.”

Off-label prescribing is already common and becoming more so. By some estimates, as many as one-half of all prescriptions are for off-label uses. An AMA study estimated that 40% to 60% of prescription drugs were given for unapproved uses. According to one survey, off-label prescribing of top-selling drugs doubled from 1998 to 2003. Another study indicated that most hospital patients receive at least one drug off label. And in some fields, the number is higher than in others. For example, according to the GAO, off-label prescribing accounts for 90% of cancer drug use, 80% of pediatric drug use, and 80% to 90% of drugs used to treat rare conditions.

Despite the frequency of off-label prescribing, the FDA has shown little interest in determining whether off-label uses are safe and effective. Rather than monitoring post-approval drug safety, the FDA has devoted its resources to new drug approval. According to a recent study, the

102. Id.
104. According to the FDA: “These uses are not approved by the FDA. No company has sent the FDA scientific proof that (Cytotec) is safe and effective for these uses. There can be serious side effects, including a torn uterus . . . .” Young, supra note 97 (quoting FDA, Misoprostol (Marketed as Cytotec) Information (May 2005), http://www.fda.gov/cder/drug/infopage/misoprostol/default.htm).
105. Radley et al., supra note 10, at 1021.
106. Id.
107. Id. at 1023.
108. Id. at 1026.
110. Angell, supra note 7, at 204.
111. Tansey, supra note 4; see also Angell, supra note 7, at 204.
112. Moyer, supra note 6, at 931.
113. Id. at 930.
115. Radley et al., supra note 10, at 1021.
FDA focuses on the market entry of new drugs "rather than regulating physician’s prescribing practices, allowing off-label use of medications for indications beyond those formally evaluated by the manufacturer" and often not supported by scientific evidence.\textsuperscript{116}

Of course, the American public is unaware of the prevalence of off-label prescribing. Indeed, most of us assume that every prescription is for an FDA-approved use.\textsuperscript{117} While we would want to know that many of our prescriptions are not for FDA-approved uses, we are often not given that information.\textsuperscript{118} In contrast to the FDA requirement of informed, written consent for all phases of its approval trials, there is no FDA requirement of informed consent to off-label prescriptions which the FDA does not regulate at all.\textsuperscript{119} As one scholar observed:

[I]nnovative therapies not undertaken as part of a study protocol escape the special federal requirements governing informed consent. This arrangement seems paradoxical. Formal study protocols have a number of different safeguards that apply to research activities. In contrast, when physicians use novel procedures or technologies in treating individual patients, they face little supervision of their activities . . .

Thus, physicians routinely, and often appropriately, deviate from the directions contained in approved prescription drug labeling. . . . Again, paradoxically, patients receive the least regulatory protection in those cases where they may need it the most—namely, when individual physicians may haphazardly try out a different technique under the guise of providing innovative therapy.\textsuperscript{120}

This practice benefits the drug industry. Given the profitability of the industry, drug companies strive to maximize sales of their prescription drugs. To reduce the time and money spent obtaining FDA approval, the manufacturer will usually seek approval for only a few uses.\textsuperscript{121} But once the FDA approves a drug for one, narrow use, the manufacturer will understandably want to expand this small market by

\textsuperscript{116} Id.
\textsuperscript{117} Tansey, supra note 4; Harris Poll, supra note 4.
\textsuperscript{118} See infra Part I.B.1.
\textsuperscript{119} Salbu, supra note 2, at 204 n.141 ("[T]his is a very uncontrolled part of medical practice. Doctors are doing uncontrolled experimentation in their own practices, and the American people are being experimented on because the drugs aren't being tested adequately." (quoting Paul D. Stolley, Chair of Epidemiology and Preventative Medicine, University of Maryland School of Medicine)). As Dr. Sidney Wolf of Public Citizen observed, "[H]uge numbers of people are going to be made guinea pigs for unapproved uses of drugs." O'Reilly & Dalai, supra note 16, at 307; see also Beck & Azari, supra note 2, at 85-87 (explaining that federal regulations requiring informed consent for FDA trials do not apply to off-label treatments).
\textsuperscript{121} Oates, supra note 37, at 1280; see Angell, supra note 7, at 158-61 (discussing the example of Neurontin, approved for epilepsy but marketed to doctors for pain and anxiety).
encouraging doctors to prescribe the drug for additional, off-label uses.\(^2\) As the following discussion shows, this is where the industry’s multi-billion-dollar marketing campaign pays off.

**B. PHARMACEUTICAL MARKETING AND ITS REGULATION**

Pharmaceutical marketing is the largest item in the drug industry’s enormous budget.\(^3\) As reported in the 2005 *Presidential Report of the National Association of Attorneys General*, the industry spent $76.5 billion on marketing to physicians in 2003.\(^4\) While estimates vary,\(^5\) one recent study concluded that the drug companies spend more than $30,000 on each doctor each year.\(^6\) Although drug companies cite the high cost of research and development (R&D) to explain the soaring price of prescription drugs,\(^7\) the industry spends “almost twice as much on marketing alone as on R&D.”\(^8\) For example, in 2002, when the ten U.S. drug companies on the Fortune 500 list had combined international sales of $217 billion, they spent 14% of that on R&D, 31% on marketing and administration, and enjoyed a profit margin of 17%.\(^9\)

Promoting off-label uses seems to be a critical strategy in this marketing campaign.\(^10\) According to proponents, off-label marketing serves public policy in several respects. First, off-label information is necessary to ensure that patients receive the most effective treatment,\(^11\) and the drug companies are in the best position to provide doctors with that information.\(^12\) Given the vastness of medical literature, even the

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124. Id. at 32 (defining “marketing to physicians” as including: advertising in medical journals, providing educational materials to doctors, providing product samples, fielding sales representatives, entering into consulting agreements with doctors, sponsoring continuing medical education (CME) programs and other promotional seminars and presentations, and providing entertainment, meals, and gifts).


128. Nat’l Ass’n of Attorneys Gen., *supra* note 41, at 22 (quoting Marcia Angell). “In 2003, the top ten drug companies spend 14% of revenue on research and development, and 34% of revenue on marketing and administration.” Id. at 7. In other words, for every dollar made in sales, the industry spent thirty-four cents on marketing and administration and fourteen cents on developing new products. Id. at 7.


130. Id. at 156–57; see infra Part I.B.1.


most dedicated doctor will inevitably fall behind. In sponsoring legislation to liberalize restrictions on off-label promotion, Senator Bill Frist, a heart surgeon, explained: "If a conscientious doctor were to read two medical articles before retiring each night, he would have fallen 550 years behind in his reading at the end of the first year." Second, promoting off-label uses should reduce drug prices since increased sales volume will enable the drug companies to lower their prices. Third, off-label marketing saves costs by eliminating expensive FDA trials and the lengthy FDA-approval process. Finally, doctors serve as learned intermediaries who are best able to evaluate the information and insure that patients receive appropriate treatment.

On the other hand, critics charge that off-label promotion creates significant risks. The drug companies completely avoid the responsibility for establishing that a drug is safe and effective for the off-label use they are promoting. Drug companies have no incentive to conduct the rigorous safety and efficacy studies the FDA requires. Indeed, they will be tempted to seek approval for a "cheap, narrow indication and the next day begin selling the drug for multiple, broad, and profitable other indications." For some drugs, the majority of the sales are off-label. The validity of the drug-company research conducted outside of the FDA oversight process is suspect since the companies are financing the research and will directly profit from positive results creating potential conflicts of interest. Drug company research emphasizes the positive features and omits information about risks and contraindications. For this reason, the doctor's role as a learned intermediary is severely

133. O'Reilly & Dalal, supra note 16, at 303; Ascroft, supra note 132, at 99.
135. Ford, supra note 100, at 434.
136. O'Reilly & Dalal, supra note 16, at 304; Salbu, supra note 2, at 195.
137. Ascroft, supra note 132, at 99; Ford, supra note 100, at 434; see infra notes 435-39 and accompanying text (explaining the learned intermediary doctrine).
138. Henry, supra note 61, at 369; Moyer, supra note 6, at 928; Ford, supra note 100, at 434.
139. Radley et al., supra note 10, at 1021; Salbu, supra note 2, at 205; Ascroft, supra note 132, at 100; Ford, supra note 100, at 434. Indeed, the FDA itself formerly argued that allowing promotion of off-label uses "would erode the statutory standard of proof of drug efficacy, diminish the use of evidence based medicine, and 'could result in harm to patients form unstudied uses that actually lead to bad results, or that are merely ineffective.'" O'Reilly & Dalal, supra note 16, at 300 (quoting Janet Woodcock, Lecture to Drug Information Association, A Shift in the Regulatory Approach (June 23, 1997)); see also Gordon, supra note 55, at 942.
142. Ford, supra note 100, at 434.
143. Id. at 435.
144. Id.
compromised. Today, rather than serving as a learned intermediary, a doctor is often a misled intermediary. Moreover, there is no evidence that drug companies will reduce the cost of widely used drugs. Quite the opposite is true. For example, the price of the top-selling allergy pill, Claritin, was raised thirteen times over five years, an increase of more than 50%—more than four times the rate of inflation.\textsuperscript{45}

While, as explained above, the FDA does not regulate off-label prescribing, it has attempted to regulate off-label marketing.\textsuperscript{46} The industry challenged the ban, arguing that it prevented dissemination of valuable information about off-label uses to doctors and therefore deprived patients of needed treatments.\textsuperscript{47} In response, in 1997, Congress passed the Food and Drug Administration Modernization Act ("FDAMA") so that drug companies could distribute reprints of independent, peer-reviewed, journal articles about off-label uses.\textsuperscript{48} But to come within this provision, the manufacturer was required to seek FDA approval of the new use within a specified time.\textsuperscript{49} The legislative intent was to enable the drug industry to distribute the most reliable research to doctors so patients could receive necessary treatments, but require the FDA to police the process to ensure that the new use was safe and effective.\textsuperscript{50}

Critics challenged the FDAMA claiming it unduly restricted the industry’s freedom of speech and thus violated the First Amendment.\textsuperscript{51} The challenge was initially successful,\textsuperscript{52} but in 2000 the D.C. Circuit dismissed the case as moot because both sides agreed that the FDAMA did not give the FDA independent authority to regulate speech.\textsuperscript{53} As the court explained, "[T]he dispute between the parties has . . . disappeared before our eyes."\textsuperscript{54} But the court cautioned that its view should not be taken as a criticism or disagreement with the lower court’s holding that the FDAMA restrictions on marketing violated the First Amendment. As the circuit court stated: "[W]e certainly do not criticize the reasoning or conclusions of the district court . . . [W]e do not reach the merits of the district court’s First Amendment holdings and part of its injunction
INFORMED CONSENT

still stands.\textsuperscript{55}

Since this ruling, the FDA has maintained that it lacks authority to regulate drug company speech.\textsuperscript{158} As a result, the FDAMA guidelines restricting off-label marketing are not being vigorously enforced.\textsuperscript{157} Indeed, one of the lawyers who challenged the FDAMA restrictions was appointed to oversee the FDA's effort to determine whether it should give manufacturers more leeway to promote off-label uses.\textsuperscript{158} Daniel Troy, a prominent First Amendment lawyer who helped the Washington Legal Foundation challenge the FDAMA restrictions, became general counsel to the FDA.\textsuperscript{159} As Dr. Michael Wilkes, Associate Dean of the School of Medicine at the University of California, Davis and a national authority on off-label prescribing and promotion, observed, "They [the FDA] certainly are backing off."\textsuperscript{160}

Given the billions of dollars involved in prescription drugs and their promotion, it is not surprising that abuses have occurred. In the late 1990s, a lawsuit exposed some of the most egregious practices.\textsuperscript{161} Dr. Joseph Gerstein, who was in charge of the formulary at a large Massachusetts Health Maintenance Organization (HMO), was offered a $20,000 "educational grant" by TAP Pharmaceuticals to reverse his decision to exclude TAP's drug.\textsuperscript{162} Dr. Gerstein refused and reported the incident to government investigators.\textsuperscript{163} TAP responded by raising the stakes. According to Dr. Gerstein, in the end TAP was offering almost half a million dollars in incentives.\textsuperscript{164} TAP's plan was to sell the drug at a discount or to give doctors free samples and then encourage doctors to bill Medicare and patients at the full price.\textsuperscript{165} By one estimate, this scheme would enable a doctor with thirty patients using TAP's drug to earn $50,000 per year.\textsuperscript{166}

Not all doctors were as honest as Dr. Gerstein. The federal investigation revealed that TAP had rewarded doctors with generous inducements, including vacations at resorts where activities included golf, skiing, and white-water rafting.\textsuperscript{167} Ultimately, four urologists pled guilty

\textsuperscript{155} Id. at 337 n.7.
\textsuperscript{156} Adams & Young, supra note 55.
\textsuperscript{157} Id.
\textsuperscript{158} Id.
\textsuperscript{160} Adams & Young, supra note 55.
\textsuperscript{161} Angell, supra note 7, at 130-32; Grieder, supra note 37, at 10-11.
\textsuperscript{162} Grieder, supra note 37, at 10-12.
\textsuperscript{163} Id. at 10.
\textsuperscript{164} Id.
\textsuperscript{165} Id. at 11.
\textsuperscript{166} Kassirer, supra note 126, at 41.
\textsuperscript{167} Id. at 13.
to fraud, twelve TAP managers were indicted on various charges, and TAP settled by paying a fine of $875 million, “including the largest criminal fine ever paid in a health-care fraud case.”

In response to the TAP case, the medical community, the drug industry, and federal regulators took steps to curtail the worst abuses. In 2000, the AMA issued voluntary guidelines for doctors accepting gifts from drug companies. In 2002, the pharmaceutical industry through its association, PhRMA, adopted similar guidelines. In 2003, the Office of the Inspector General (OIG) of the Department of Health and Human Services warned that the federal anti-kickback laws could be triggered by excessive gift-giving by drug companies to doctors. Although the initial OIG warning was broad, the OIG responded to strong lobbying efforts by the AMA and PhRMA. The final version essentially reflects the AMA and PhRMA guidelines.

While these measures have promise, they have failed to solve the marketing-abuse problem for two main reasons. First, of course, they are only voluntary and thus unenforceable. The OIG specifically states that its guidelines are only intended to present voluntary guidance to the industry, not to provide binding standards. A recent report in the Journal of the American Medical Association concluded that:

[T]he guidelines produced by these various groups and organizations are not sufficiently stringent and do not adequately uphold a professional commitment to patient welfare and research integrity. None of these groups establishes monitoring mechanisms or pinpoints responsibility for compliance.

Second, the AMA, PhRMA, and OIG’s guidelines contain a major

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168. Greider, supra note 37, at 11.
169. Angell, supra note 7, at 128, 132.
170. Id. at 128–29, 132, 137.
171. Id. at 129.
172. Kassirer, supra note 126, at 201.
173. Id.
174. In 2004, California Governor Schwarzenegger signed into law a bill requiring compliance with the guidelines of the Office of Inspector General (OIG) and PhRMA. Cal. Health & Safety Code § 119402 (West 2006) (adopting the guidelines); Nat’l Ass’n of Attorneys Gen., supra note 41, at 89. But while this Fair Drug Marketing Law is a step in the right direction, it leaves some room for improvement since it recognizes important exceptions which threaten to undermine—if not gut—the law’s effectiveness. Specifically, exempt activities include: (1) drug samples for free distribution to patients; (2) financial support for medical education forums and scholarships; and (3) legitimate payments for consultants at fair market value. § 119402(d)(2)-(3); Nat’l Ass’n of Attorneys Gen., supra note 41, at 90; see infra Part I.B.2-6.
177. Brennan, supra note 39, at 430.
loophole: they do not apply to "education." This exception is particularly important for the drug companies to expand off-label prescribing and increase sales. The link between education and off-label prescribing was explained by Marcia Angell, M.D., former editor-in-chief of the New England Journal of Medicine, and current member of Harvard Medical School’s Department of Social Medicine:

[I]f drug companies can somehow convince doctors to prescribe drugs for off-label uses, sales go up. The problem is how to get around the law prohibiting marketing for those uses.

That is where "education" comes in. If drug companies pretend they are merely informing doctors about other potential uses, they can circumvent the law. And that is what they do. They sponsor make-believe education, and often buttress it by references to flimsy research studies they sponsor.

In short, by calling their marketing campaigns "education" the drug companies can evade even the toothless restrictions adopted by the AMA, PhRMA, and OIG.

The following discussion will describe how the drug industry’s promotion of prescription drugs creates conflicts of interest for doctors prescribing both on- and off-label. Specifically, drug companies sponsor research which they then present to doctors at free continuing medical education programs. They retain doctors as speakers and consultants to publicize and promote these uses. They deploy armies of representatives (detailers) to doctors’ offices with free samples to encourage prescribing. And they shower the doctors with gifts, meals, and travel expenses to generate a desire to reciprocate. In addition to promoting approved uses, the companies also use these strategies to expand a drug’s market to off-label uses. After summarizing a case illustrating how these tactics work together to expand off-label prescribing, each will be discussed separately in greater detail.

1. An Illustration of Pharmaceutical Marketing Abuses: The Neurontin Case

The illegal scheme to promote the epilepsy drug Neurontin (gabapentin) for many off-label uses illustrates the marketing strategy

178. Angell, supra note 7, at 138.
179. Harvard Medical School, Department of Social Medicine, Faculty, Marcia Angell, http://www.hms.harvard.edu/dsm/WorkFiles/html/people/faculty/MarciaAngel.html (last visited Apr. 1, 2007).
180. Angell, supra note 7, at 137.
182. See infra Part I.B.3; see also Stoffelmayr, supra note 15, at 280.
184. See infra Part I.B.5.
the drug companies pursue. Whistle-blower David P. Franklin produced thousands of pages of internal documents showing Parke-Davis (later acquired by Pfizer) promoted Neurontin by paying academic experts to sign on to shoddy research purporting to show that the drug was effective for other uses. This "publications strategy" was designed to pump up the sales of the drug which was "approved by the FDA in 1994 for a very narrow use—to treat epilepsy as an add-on when other drugs failed to control seizures." First, Parke-Davis sponsored tiny studies. Then it paid medical education and communication companies (MECCs) to prepare journal articles and find academic researchers to sign them. Some academic "authors" were paid $1000. Sometimes an "author" was difficult to recruit. As one progress report from the MECC to Parke-Davis complained, "Author interested; still playing phone tag..." Once the company had its "research" ready, it widely disseminated the reports to doctors and touted the results at educational meetings and conferences around the country. It allegedly paid dozens of doctors tens of thousands of dollars each to speak at such programs and paid the doctors in the audience as "consultants." According to the New York Times, one doctor, formerly at the University of Florida, received more than $300,000 over a three-year period. This promotional scheme was a huge success. The New York Times reported that prescriptions increased about 70% after dinner meetings.

And so, Neurontin became a blockbuster drug. In 2003, it had sales of $2.7 billion, about 80% of these prescriptions were for off-label uses including "bipolar disorder, post-traumatic stress disorder, insomnia, restless legs syndrome, hot flashes, migraines, and tension headaches."

186. ANGELL, supra note 7, at 157-61.
187. Id. at 157-58; Alicia Mack, Examination of the Evidence for Off-Label Use of Gabapentin, 9 J. MANAGED CARE PHARMACY 559, 562 (2003) (finding that the majority of medical literature on Neurontin was composed of open-label studies evaluating small numbers of patients, with a lack of randomized controlled clinical trials).
188. ANGELL, supra note 7, at 158.
190. ANGELL, supra note 7, at 158-59; KASSIRER, supra note 126, at 32-53.
191. KASSIRER, supra note 126, at 32.
192. ANGELL, supra note 7, at 159 (capitalization in the original).
193. Id.
195. KASSIRER, supra note 126, at 28.
196. ANGELL, supra note 7, at 160.
197. Id.; accord Mack, supra note 187, at 559 (noting that 95% of patients in a managed Medicaid plan were using Neurontin for off-label diagnoses); Radley et al., supra note 10, at 1023, 1024 tbl.2 (finding that in a study of clinical prescribing habits, 83% of Neurontin (gabapentin) uses were off-label).
Of course, no reliable evidence showed that it was effective for treating any of these conditions. Furthermore, in the treatment of neuropathic pain, one of the few off-label applications of Neurontin supported by valid evidence, Neurontin was no more effective than its much less expensive competitors. Pfizer pled guilty to illegal marketing and agreed to pay $430 million to resolve civil and criminal charges. But with sales totaling $2.7 billion, one expert described the fine as "small potatoes."

Unfortunately, Neurontin is not an isolated example. By 2003, Eli Lilly had settled three lawsuits alleging that it had over-marketed Prozac—approved as an antidepressant—for off-label uses including migraines, Tourette’s syndrome, and heart pain. In July 2005, a drug company employee filed a whistle-blower lawsuit alleging Genentech illegally marketed its cancer drug Rituxan as a treatment for rheumatoid arthritis. In December 2005, Eli Lilly pled guilty to federal charges and agreed to pay $36 million to settle a lawsuit charging that it illegally marketed its Evista osteoporosis drug as a treatment for breast cancer and heart disease. In the fall of 2006, InterMune agreed to a settlement with the federal government of $36.9 million based on allegations that it illegally promoted the off-label use of Actimmune to treat pulmonary fibrosis. In September 2006, Schering-Plough Corp. agreed "to plead guilty to conspiracy and to pay $435 million in criminal and civil fines to end a federal probe into the marketing of some drugs for unapproved uses."

The Neurontin case illustrates the industry’s coordinated marketing strategy. The following discussion considers several of its tactics: (1) funding research; (2) sponsoring continuing medical education; (3) employing consultants; (4) detailing and sampling; and (5) providing gifts, meals, and travel expenses.

198. See Angell, supra note 7, at 160-61; Mack, supra note 187, at 562; Radley et al., supra note 10, at 1024 tbl.2 (finding that 66% of off-label Neurontin uses had little or no scientific support).
199. See Mack, supra note 187, at 562 & tbl.3, 563 (finding Neurontin to be five to twenty times as expensive as amitriptyline and nortriptyline, and no more effective).
201. Angell, supra note 7, at 161 & n.7.
202. Adams & Young, supra note 141.
205. Pollack, supra note 22.
2. Funding Research

While the Neurontin example may be extreme, evidence suggests that other post-approval research is similarly shoddy and serves primarily as a tool to promote off-label uses and to increase sales. As Dr. Angell explained, drug companies promote off-label uses through professional education based on company-sponsored research:

You do that by carrying out “research” that falls way below the standard required for FDA approval, then “educating” doctors about any favorable results. That way, you could circumvent the law. You could say you were not marketing for unapproved uses; you were merely disseminating the results of research to doctors—who can legally prescribe a drug for any use. But it would be bogus education about bogus research. It would really be marketing.

As the Neurontin example illustrates, sometimes drug companies procure research by simply hiring a ghost writer. As the deputy editor of the Journal of the American Medical Association explained, drug companies want a non-company person listed as the author to enhance credibility. One experienced ghost writer explained that while some authors carefully review the drafts, others simply sign their names. One doctor who declined a drug company’s solicitation to sign an article described his experience as a warning to others.

In addition to ghost writing articles, the industry has a number of other arrangements to generate “research” about off-label uses. As discussed above in Part I.A, to obtain FDA approval for a new drug, the manufacturer is required to conduct three phases of clinical trials, obtain the patients’ informed consent, and report the results to the FDA. This pre-approval research is referred to as Phase I through III research, reflecting the stage in the approval process when it is conducted. After obtaining approval, the company may conduct additional research. This post-approval research is referred to as “Phase IV” research. But unlike Phase I through Phase III research, most Phase IV research is not subject to FDA standards or the informed consent requirement. This

207. See Angell, supra note 7, at 157, 161–64 (discussing “the use of flimsy Phase IV clinical research for marketing purposes”).
208. Id. at 157.
209. See supra notes 190–92 and accompanying text; see also Kassirer, supra note 126, at 31–33.
211. Kassirer, supra note 126, at 33.
212. Id.
213. Id.
214. See Namioshi, supra note 55, at 9; Beck & Azari, supra note 2, at 75; supra notes 54–66 and accompanying text.
216. Id.
Phase IV research accounted for at least 25% of all clinical trials conducted in 2002, and the number of these trials "is growing much faster than [the number] of Phase I through III trials." Phase IV research may be conducted for several reasons. First, the research may be conducted to determine whether the drug is effective for additional treatments and to seek FDA approval for them. This category of Phase IV research is subject to the same restrictions as Phase I through Phase III research since the requirements for adding a new use to the label are the same as for initial new drug approval. Because of the expense and time required to comply with these standards, this type of Phase IV research is rarely conducted. Second, the research may be conducted to study side effects that were undetected in the initial trials. For example, where a drug received expedited approval, the FDA may require post-market studies. Finally, the research may be conducted to market the drug to doctors, as in the Neurontin case.

A typical Phase IV arrangement in this last category is a surveillance study where the drug companies pay the doctors to prescribe a particular drug and to answer a few short questions about the treatment. These trials are not randomized and have no comparison group, "so it is usually impossible to draw any reliable conclusions." To critics, these arrangements are "just excuses to pay doctors to put patients on a company's already-approved drug." An article by Dr. David Kessler, then head of the FDA, reported on a "study" where a drug company recruited 2500 doctors to enroll twelve patients each in a trial of a new blood pressure drug and paid the doctors $1050 for participating. The trial was not conducted to study the drug, but only to increase sales.

217. See Beck & Azari, supra note 2, at 85-86 (discussing off-label use); Noah, supra note 120, at 392-93 (discussing experimental use).
218. ANGELL, supra note 7, at 161.
219. Id.
220. Oates, supra note 37, at 1284-85.
221. Id. at 1283 (explaining why this type of Phase IV research is uncommon).
222. ANGELL, supra note 7, at 162.
223. Id. at 162-63. Unfortunately, according to an investigation by the Government Accountability Office (GAO), these studies are often delayed and the FDA lacks an effective process to enforce these conditions on approval. Andrew Bridges, Probe Finds FDA Needs More Muscle, S.F. CHRON., Apr. 24, 2006, at A2; see also Andrew Bridges, Companies Failing to Do Tests on Expedited Drugs, FDA Says, S.F. CHRON., Mar. 4, 2006, at A8.
224. ANGELL, supra note 7, at 163-64.
225. Id. at 163.
226. Id. at 163.
227. Id. at 30, 39, 164. The United States Department of Health and Human Services has recognized the problem of doctors failing to disclose their financial incentives for patient recruitment. See Kapp, supra note 41, at 256-57.
228. GREIDER, supra note 37, at 82.
229. See id.
Drug companies compensate doctors for engaging patients in clinical trials.230 According to Dr. Jerome Kassirer, former editor-in-chief of the New England Journal of Medicine, drug companies pay “$2000 to $4000 for enrolling individual patients into drug trials, and offer additional bonuses of $2000 to $3000 when enrollment slows down over the holiday season.”231 A busy physician can easily earn tens of thousands of dollars a year from such patient enrollments.232 In instructing their sales representatives about the importance of Phase IV trials, one company candidly admonished: “Make no mistake about it: The [name of drug omitted] study is the single most important sales initiative of 1993. . . . If at least 20,000 of the 25,000 patients involved in the study remain on [the drug], it could mean up to a $10,000,000 boost in sales.”233 In other words, this research is not research in the conventional sense. In reality, it is marketing.

In addition to paying doctors to prescribe drugs under the guise of research, the drug companies also hire private, for-profit research organizations (CROs) to run Phase IV trials.234 Some of these CROs are actually owned by advertising agencies, which is itself revealing.235 Since the 1990s, the increasing number of trials run by CROs, rather than academic research institutions, has enabled the drug companies to control the research and the publication of results.236

The industry pays for research through other arrangements as well.237 For example, the 2003 supplement to the Primary Care Companion to the Journal of Clinical Psychiatry contains several articles promoting the off-label use of Provigil, a drug approved for narcolepsy, for other medical conditions including an unrecognized ailment described as “executive disfunction.”238 The supplement was paid for by the drug’s manufacturer, Cephalon, which also paid the lead authors of all eight papers in the supplement through honoraria, consultant agreements, speaking engagements, or research funds.239 As Dr. Kassirer concluded, “This supplement is a shameful marketing tool.”240

Unfortunately, but perhaps not surprisingly, drug-company-

232. Id. at 9; see also Kurt Eichenwald & Gina Kolata, Drug Trials Hide Conflicts for Doctors, N.Y. Times, May 16, 1999, at A1 (reporting on doctor recruitment of patients, the bounties paid per patient, and the lack of controls or expertise in these studies).
233. Greider, supra note 37, at 82–83 (emphasis added).
235. Id. at 166–67.
236. Greider, supra note 37, at 79.
238. Kassirer, supra note 126, at 28.
239. Id.
240. Id.
sponsored research is biased and unreliable. In a blind study of seventy articles about one type of drug, researchers contacted authors to determine whether drug companies had supported their research.\textsuperscript{241} The survey found that researchers who had financial ties to the drug's manufacturer gave the most positive reports on the drug.\textsuperscript{242} This biased research prevents doctors from making informed decisions about the drugs they are prescribing.\textsuperscript{243} As the editors of a major medical journal lamented: "How tainted by commercial conflicts has medicine [and its literature] become? Heavily, and damagingly so, is the answer."\textsuperscript{244}

In addition to supporting studies that favor positive results,\textsuperscript{245} the industry further skews the research in several ways.\textsuperscript{246} Sometimes the research reports only the positive part of the data and ignores the rest.\textsuperscript{247} For example, a clinical trial sponsored by the maker of Celebrex purportedly showed that it caused fewer side effects than older arthritis drugs.\textsuperscript{248} The \textit{Journal of the American Medical Association} published these results along with a favorable editorial.\textsuperscript{249} But these results were based on the first six months of a year-long trial which ultimately showed that Celebrex was not superior to the older drugs.\textsuperscript{250} The editor was understandably furious to learn that the company had the data for the second six months when it submitted the manuscript touting the purported benefits.\textsuperscript{251}

Another approach is to support studies comparing the drug to a placebo rather than comparing it to the best available treatment.\textsuperscript{252} Some studies compare the company drug to another that does not really fit the symptoms at issue.\textsuperscript{253} Dosages can be rigged to favor the company's drug over the competitor.\textsuperscript{254} Alternatively, the duration of treatment can be selected to favor the company's drug.\textsuperscript{255} Sometimes the studies limit the

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\textsuperscript{241} See id. at 79-80.
\textsuperscript{242} Id.
\textsuperscript{243} See Kapp, supra note 41, at 259-61.
\textsuperscript{244} Id. at 259 (quoting \textit{Just How Tainted Has Medicine Become}, 359 \textsc{Lancet} 1167, 1167 (2002)).
\textsuperscript{245} Kassirer, supra note 126, at 167.
\textsuperscript{246} Angell, supra note 7, at 107-09.
\textsuperscript{247} Id. at 108. In some cases, manufacturers prohibited or delayed publication of research results. See Thomas Bodenheimer, \textit{Uneasy Alliance—Clinical Investigators and the Pharmaceutical Industry}, 342 \textsc{New Eng. J. Med.} 1539, 1541-42 (2000).
\textsuperscript{248} Angell, supra note 7, at 108-09; Fred E. Silverstein et al., \textit{Gastrointestinal Toxicity with Celecoxib vs Nonsteroidal Anti-Inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis}, 284 \textsc{JAMA} 1247, 1253-54 (2000).
\textsuperscript{249} Angell, supra note 7, at 109; David R. Lichtenstein & M. Michael Wolfe, \textit{COX-2-Selective NSAIDs: New and Improved?}, 284 \textsc{JAMA} 1297 (2000).
\textsuperscript{250} Id., at 109; Greider, supra note 37, at 83-84, 102.
\textsuperscript{251} Kassirer, supra note 126, at 167.
\textsuperscript{252} Id.
\textsuperscript{253} Id.; see also Greider, supra note 37, at 83.
\textsuperscript{254} Kassirer, supra note 126, at 167.
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monitoring of side effects. And sometimes the “principal investigator” does not design the study, but follows the company’s prepackaged instructions. Another tactic is to repeatedly publish positive results. As Dr. Angell explained:

>[The FDA] has no control over this selective publishing. The practice leads doctors to believe that drugs are much better than they are, and the public comes to share this belief, on the basis of media reports. There is a general inflation in the notion of the good that drugs can do (and a deflation in concern about side effects).

In short, drug companies have developed a number of strategies to increase sales by generating biased and substandard “research” that exaggerates the benefits and minimizes the risks of their products.

Medical journals cannot be trusted to screen articles for reliability for two reasons. First, drug companies rig the results in ways that often cannot be detected even by experts. Second, journal editors may themselves be biased. Indeed, conflicts of interest on editorial boards are ubiquitous. Most journals have only part-time editors who may have financial ties to drug companies. When Dr. Kassirer recommended to one journal that editors should not handle articles if they had financial relationships with companies producing featured products, his recommendation was met with derision. As the editor-in-chief explained, “[I]f he adopted such a policy, he would have no editorial board!”

Dr. Angell, who spent two decades at the New England Journal of Medicine, described the growing problem of biased, company-sponsored research:

The staple of the journal is research about causes of and treatments for disease. Increasingly, this work is sponsored by drug companies. I saw companies begin to exercise a level of control over the way research is

256. Id.
257. Id.
258. Angell, supra note 7, at 112.
259. Id.
260. Id. at xviii-xix.

An... egregious set of events occurred at Neuropsychopharmacology, which recently published a favorable assessment of a controversial new treatment for depression resistant to conventional therapies. Left unmentioned was that eight of the nine authors serve as consultants to the company that makes the device used in the therapy. The ninth works directly for the company. Just to make things particularly incestuous, the lead author of the study is the journal’s editor and a consultant to the company.

Id.
262. Kassirer, supra note 126, at 89.
263. Id.
done that was unheard of when I first came to the journal, and the aim was clearly to load the dice to make sure their drugs looked good. . . . There are other ways to bias research, and not all of them can be spotted, even by experts. Obviously, we rejected such papers when we recognized them, but often they would turn up in other journals. Sometimes companies don’t allow researchers to publish their results at all if they are unfavorable to the companies’ drugs. As I saw industry influence grow, I became increasingly troubled by the possibility that much published research is seriously flawed, leading doctors to believe new drugs are generally more effective and safer than they actually are.264

In short, while rigorous standards apply to the clinical trials necessary for FDA approval, post-approval research is highly suspect. It is often a disguised vehicle to pay doctors to prescribe a drug. It is manipulated by drug companies to produce unjustifiably rosy reports to support promotional campaigns to expand market share. As the next section explains, once the companies have procured the “research” they want to promote their products, they deliver it to doctors at drug-company sponsored educational programs.

3. Sponsoring Continuing Medical Education

Most states require continuing medical education (CME), and the drug companies happily provide it.265 In 2001, drug companies paid 60% of the costs of CME, and that percentage has increased.266 Many doctors get substantial amounts of their CME from free, drug-company-sponsored programs largely taught by doctors who are paid members of the drug-company’s speakers’ bureaus.267 Drug companies spend millions on educational grants. In 2004, twenty-three drug companies spent $1.47 billion on these grants, a 20% increase from the 2003 total.268 A congressional investigation recently concluded that these grants are sometimes steered by marketing executives to doctors and groups promoting off-label uses.269

Attendance at company-sponsored events often includes dinners in expensive restaurants and junkets to luxurious resorts.270 According to one estimate, the industry hosted more than 300,000 events in 2000,271 four times more than in 1993.272 This investment pays off since doctors prescribe more of the sponsors’ drugs after these meetings.273 Remember,

264. ANGELL, supra note 7, at xviii–xix.
265. Id. at 138–39; KASSIRER, supra note 126, at 15–16.
266. ANGELL, supra note 7, at 139; see also KASSIRER, supra note 126, at 16.
267. NAT’L ASS’N OF ATT’YS GEN., supra note 41, at 40.
268. Gardiner Harris, Drug Makers Scrutinized Over Grants, N.Y. TIMES, Jan. 11, 2006, at Cl.
269. Id.
270. ANGELL, supra note 7, at 141.
271. Id. at 142.
272. GREIDER, supra note 37, at 71.
273. ANGELL, supra note 7, at 141. A recent example illustrates the integration of several of these
these "education" expenses fall outside the guidelines restricting drug company marketing. And, according to the FDA, CME-sponsored activities are not subject to the restriction for marketing off-label uses. Moreover, drug companies determine what is education or research and what is marketing. According to the Inspector General, "The manufacturer should determine whether the funding is for bona fide educational or research purposes." Not surprisingly, the industry does not believe that sponsorship of CME programs is marketing.

As part of their educational programs, drug companies hire private, for-profit MECCs to plan the meetings, prepare materials, and hire speakers. By contracting with MECCs, the drug companies adhere to the PhRMA and AMA guidelines against directly funding individual expenses. But some MECCs are actually owned by advertising agencies, demonstrating the connection between "education" and marketing. The MECC's goal is to promote the drugs of the drug-company sponsor. As one candidly explained, it develops "educational programs that foster early product acceptance... Programs are designed to gain a higher rate of acceptance at the launch of a new product and to increase return on investment." Another explained, "Medical education is a powerful tool that can deliver your message to key audiences and get those audiences to take action that benefits your product."

The industry argues that these educational programs provide doctors with the latest information they need to practice medicine and thus benefit both doctors and their patients. But the information provided at industry-sponsored programs is biased. According to Dr. Arnold Relman, editor-in-chief emeritus of the New England Journal of Medicine, "[T]hese courses often present information that is biased in favor of the companies that funded the courses, that they sometimes provide information that lacks hard scientific facts, and are not even-

274. ANGELL, supra note 7, at 137–38.
275. NAT'L ASS'N OF ATTORNEYS GEN., supra note 41, at 36.
276. ANGELL, supra note 7, at 138.
277. Id.
278. Id.
279. ANGELL, supra note 7, at 139; KASSIRER, supra note 126, at 93; see also GREIDER, supra note 37, at 71.
280. KAPP, supra note 41, at 248–49.
281. ANGELL, supra note 7, at 139.
282. KASSIRER, supra note 126, at 93.
283. Id.
handed. A review by the *Journal of the American Medical Association* found that drug-company-sponsored programs “always preferentially highlighted” the sponsor’s drug, and that attendees prescribed the company’s drug more frequently after attending these programs. Indeed, drug companies admit that they track the market impact of CME expenditures and fund only those programs that increase the use of their products.

In addition to sponsoring CME programs, the drug companies underwrite professional association meetings where they sponsor free symposia. For example, at the annual meeting of the American Psychiatric Association, in addition to a $60,000 payment to the Association, drug companies spent between $200,000 and $400,000 for each of the more than fifty industry-sponsored symposia. In other words, they spent between $10 million and $20 million for this one professional meeting alone. The expense is warranted because medical conferences provide an excellent opportunity for drug companies to promote off-label uses. For example, a Knight Ridder report explained how staffed sales booths at medical conventions promoted off-label prescriptions. Specifically, at the Merck booth, representatives volunteered that Vioxx—the blockbuster, now withdrawn, arthritis drug—could be used preemptively although it was not FDA-approved for preemptive treatment. The Allergan representative volunteered that Botox was used for back pain and migraine pain although not approved for those uses. Sponsored speakers are paid handsomely for their time. Indeed, one cardiologist boasted that he earned $100,000 at a single meeting of the American Heart Association.

In sum, CME programs and professional conferences provide drug companies a forum for promoting drugs’ on- and off-label uses. While these commercial programs are frequently criticized for bias, they successfully increase prescribing by the doctors who attend. In other words, while the drug companies do not consider these programs to be “marketing” subject to regulatory and professional restrictions, the drug companies exclusively support the programs that expand their market.

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284. *Id.* at 92.
285. GREIDER, *supra* note 37, at 73.
287. KASSIRER, *supra* note 126, at 8–9, 60–61. In chapter six, Dr. Kassirer traces the connections between several associations and their drug company sponsors. *Id.* at 103–30.
288. ANGELL, *supra* note 7, at 146.
289. Adams & Young, *supra* note 141.
290. *Id.*
291. *Id.*
292. KASSIRER, *supra* note 126, at 17.
4. Hiring Consultants

By calling the doctors “consultants” or “advisors,” the companies can actually pay them to attend company-sponsored CME programs. The PhRMA guidelines address these consultancies. The guidelines require a written contract, a legitimate need for services, selection criteria, and record-keeping. Yet critics point out that in many cases, no real consulting or advising takes place. After a few hours of lectures in the morning, “consultants” still have ample time for a round of golf and a gourmet dinner. As one doctor explained, “The companies used to call it coming to dinner. Now it’s called consulting.” According to Dr. Kassirer, in many of these relationships the doctor is “asked to consult on little more than which wine to order.”

A few examples illustrate the practice. When Searle launched a campaign to boost sales of its new pain reliever Celebrex, it recruited 300 doctors for a weekend stay in Orlando, including expenses and a $500 payment for attending. If the doctors were willing to give talks about Celebrex, they could earn $500 for each talk. Not to be outdone, Merck held a one-day meeting in Boston where doctors were paid $1000 to attend as consultants. Health Learning Systems, a MECC, offered $1200 to thirty doctors to stay at the Ritz-Carlton in Phoenix to learn to use a slide set about its new drug and agreed to pay them another $1200 for each presentation the doctors gave. But these examples are dwarfed by the eye-popping $400,000 that Medtronic allegedly paid to orthopedic surgeon Dr. Thomas Zdeblick for eight days of consulting annually.

Critics contend that the PhRMA guidelines fail to correct these practices. Indeed, the PhRMA illustration of acceptable arrangements supports the criticism. Specifically, the 2002 PhRMA Code provides the following hypothetical scenario:

Question: Company A invites 300 physicians/consultants to a two-day and one-night speaker-training program at a regional golf resort. All attendees are compensated for their participation and their expenses are reimbursed... Training sessions take both days, and the Company provides for a few hours of golf and meals. Does this program conform...
to the Code? . . .

Answer: This arrangement appears to comply with the Code.

In other words, drug manufacturers disseminate the company-sponsored “research” about products at CME programs through paid speakers lecturing to paid consultants, who then return to their practices and prescribe the featured drug to their patients.

5. Detailing and Sampling

In 2001, drug companies fielded 88,000 representatives or “detailers,” one for every five to six doctors. According to one survey, the industry spent $9 billion on detailing in 2001, compared to $4.9 billion in 1996. Detailers are invariably attractive and enthusiastic young people. The New York Times reported that the drug industry recruits college cheerleaders to become detailers. Indeed, one employment firm maintains a database of cheerleaders because so many of them were going into drug sales. As they say in the industry, “You’ll never meet an ugly drug rep.”

Detailers visit frequently, often several times a week, and befriend the doctors and their staffs with free lunches, free samples, and gifts. For example, as many as ten detailers visited one small medical practice in rural Iowa in one day. And busy doctors rely on the detailers to provide information about new drugs.

Through its detailers, the industry gives away mountains of drug samples. It gave doctors almost $11 billion worth of samples in 2001, $13.1 billion in free samples in 2003, and $15.4 billion in free samples in 2004. Free samples effectively encourage doctors to prescribe an expensive, new drug even though an older and cheaper drug might be just as good or even better. As one critic observed, “Sampling effectively lowers the threshold for prescribing and taking a costly new


306. Angell, supra note 7, at 115, 126; Blumenthal, supra note 131, at 1886.


309. Id.

310. Id.

311. Angell, supra note 7, at 126, 128; see also Kassirer, supra note 126, at 7.

312. Greider, supra note 37, at 68.

313. Id. at 67.

314. Angell, supra note 7, at 115.

315. Nat’l Ass’n of Attorneys Gen., supra note 41, at 32.

316. Id.

317. Angell, supra note 7, at 129; Greider, supra note 37, at 76.
Doctors often have no knowledge of cost of the “free” drug nor any information about how it compares to an older, cheaper, generic drug. The result is that doctors prescribe expensive, on-patent drugs instead of older, cheaper alternatives. As Dr. Angell explained sampling practices:

These [samples] were almost always the newest, most expensive me-too drugs. The companies knew that when the free samples ran out, you and your doctor would be hooked on them. The drugs weren’t really free, of course. The costs were simply added on to the drug prices (these firms are not charities).

John Kitzhaber, former emergency room doctor, two-term Governor of Oregon, and Director of the Center for Evidence-Based Policy at the Oregon Health & Science University, describes how sampling drives up spending with an anecdote. A young, healthy member of his staff went to see his doctor for wrist pain. His doctor gave him a free sample of Celebrex and a prescription for it if it helped his wrist. According to Governor Kitzhaber, no evidence suggested that Celebrex, which costs $110 per month, is more effective than Ibuprofen which costs $10 per month. As he concluded, “The difference here is over $100 which did not provide a meaningful health benefit, but contributed to the escalation in health care cost.”

In addition to boosting the sales of expensive on-patent drugs over generics, sampling increases risky off-label prescribing. According to a Knight Ridder report, drug companies “have sent off-label retail sales soaring” by offering free supplies of specialty drugs to non-specialists. For example, they provided cardiologists with Prozac, approved as an antidepressant, to treat heart conditions. According to the report, in 2003, five hundred thousand Prozac prescriptions were for off-label uses. But these non-specialists are not aware of the risks of the drug, including suicide, which appeared in psychiatric journals, not cardiology journals.

A recent policy proposal published in the Journal of the American Medical Association concluded that sampling creates “a powerful

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318. GREIDER, supra note 37, at 76.
319. NAT'L ASS'N OF ATTORNEYS GEN., supra note 41, at 8, 77.
320. ANGELL, supra note 7, at 115.
321. NAT'L ASS'N OF ATTORNEYS GEN., supra note 41, at 70, 77.
322. Id. at 77.
323. Id.
324. Id.
325. Id.
326. Adams & Young, supra note 141.
327. Id.
328. Id.
329. Id.
inducement for physicians and patients to rely on medications that are expensive but not more effective” and a “tension between current marketing practices and good patient care.” It recommended that pharmaceutical samples should be prohibited and replaced by vouchers or other methods for helping low-income patients.

6. Providing Gifts, Meals, and Travel Expenses

While some physicians never accept even the most modest gift, others “eagerly accept all such industry largesse.” The American College of Emergency Physicians describes the current situation:

Gifts from industry to physicians take many forms, and may include the pens and notepads that are ubiquitous in doctors’ offices and throughout hospitals, including emergency departments; reference tools, such as sponsor-labeled copies of the Sanford Guide to antibiotic usage and even major emergency medicine textbooks; snacks and food provided to ED [emergency department] staff on duty or to residents for the regular conferences; and invitations to hear drug-company-sponsored “educational” presentations at a posh restaurant or local country club.

When sponsoring professional meetings, drug companies distribute many gifts. According to one account:

Many big professional meetings resemble bazaars, dominated by garish drug company exhibits and friendly salespeople eager to ply doctors with gifts while they pitch their companies’ drugs. Doctors wander the vast exhibit halls carrying canvas bags displaying drug company logos and brimming with goodies, munching on free food, and partaking of all sorts of free services, such as cholesterol screening and putting green practice. Instead of sober professionalism, the atmosphere of these meetings is now trade-show hucksterism.

Dr. Kassirer describes the unsolicited gifts received by one doctor in one month. They included five invitations to top restaurants, gift certificates, an all-expense paid trip to Cancún with a $1000 honorarium, and an all-expense paid trip to a resort in Phoenix with a $2000 honorarium along with $100 for incidental expenses. Both the Cancún and Phoenix offers would enable the doctor to earn more money by delivering paid lectures for the drug companies.

The drug companies contend that the 2002 PhRMA guidelines

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331. Id.
333. Id.
334. ANGELL, supra note 7, at 145; accord KASSIRER, supra note 126, at 3–5.
335. KASSIRER, supra note 126, at 4–5.
336. Id.
337. Id.
adequately addressed the problem.\textsuperscript{338} The guidelines do restrict gift giving. Specifically, they limit gifts to: "(1) items of modest value ($100 or less) if they primarily benefit patients (e.g., medical textbooks); or (2) items of minimal value if they are associated with a professional’s practice (e.g., pens, notepads)."\textsuperscript{339} But compliance with the code is voluntary.\textsuperscript{340} Moreover, the code fails to specify how often these gifts may be given—every year? every week? every day?\textsuperscript{341} And, of course, the code doesn’t apply to "education."\textsuperscript{342}

Have the PhRMA guidelines actually curtailed gift giving? Information obtained under a Vermont law documents drug company gift practices since the PhRMA guidelines were adopted. In 2002, Vermont adopted the Pharmaceutical Marketing Disclosure Law (or Gift Disclosure Law) which requires disclosure of some marketing expenditures.\textsuperscript{343} Specifically, the law requires the disclosure of "the value, nature, and purpose of any gift, fee, payment, subsidy or other economic benefit" provided in connection with marketing drugs to health-care providers.\textsuperscript{344} The Vermont Attorney General’s Office must aggregate the information and publish an annual report.\textsuperscript{345}

Despite significant exceptions that result in the understatement of actual expenditures,\textsuperscript{346} the Attorney General’s 2005 report is revealing. During FY 2004, forty-eight drug companies spent $3.11 million on fees, travel expenses, and other direct payments to Vermont health care providers, a 26\% increase from the $2.47 million spent in 2003.\textsuperscript{347} "In FY [20]04, physicians and other prescribers received 54\% of the total payments and benefits, compared with 49\% in FY 2003."\textsuperscript{348} Beginning in 2004, the drug companies were required to report the names of recipients

\textsuperscript{338} Nat’l Ass’n Of Attorneys Gen., supra note 41, at 38.
\textsuperscript{339} Id. (citing the PhRMA Code, supra note 305, at 4–5).
\textsuperscript{340} Angell, supra note 7, at 132.
\textsuperscript{341} Id.
\textsuperscript{342} Id. at 137.
\textsuperscript{344} Nat’l Ass’n Of Attorneys Gen., supra note 41, at 90–91 (citing VT. STAT. ANN. tit. 33, § 2005 (2006)).
\textsuperscript{345} Id. at 91.
\textsuperscript{346} Id. at 91–92. Specifically, the law exempts: (1) free samples intended for distribution to patients; (2) payment of compensation and expenses associated with clinical trials; (3) gifts and payments with a value under $25; (4) scholarships and support for medical students, residents, and fellows to attend medical conferences; (5) unrestricted grants for continuing medical education programs; and (6) drug rebates and discounts. Id. at 91. Moreover, the required reporting does not include expenditures on advertising or the salaries of detailers. Id. at 92.
\textsuperscript{347} Id. at 91.
\textsuperscript{348} Id.
along with the value of gifts. According to the Attorney General’s report, 426 recipients “received an aggregate amount of $1,450,758 during the last six months of FY [20]04, the [twenty-five] recipients who received the greatest amount of reportable gifts [during this period] received [$900,804].” The top ten doctors received payments between $20,000 and $80,000. On a national basis, the $3.11 million spent by pharmaceutical manufacturers on fees, travel expenses, and other direct payments in FY 2004 in Vermont would amount to $1.45 billion. Of course, these gifts were all given after the PhRMA guidelines were adopted to discourage excessive gift giving. In short, two years after the PhRMA guidelines were adopted, gifts to doctors had not decreased at all, but had actually increased significantly. And this public report is only for the tiny state of Vermont. Imagine the likely figures for California where 20,000 of the nation’s 83,000 drug detailers work.

The industry defends these practices. According to Scott Lassman, Associate General Counsel for PhRMA: “The [PhRMA] Code allows these items because they are nothing more than business courtesies that do not influence prescribing decisions. Indeed, it would be highly disrespectful to physicians to suggest that their prescribing decisions could be improperly influenced by a business courtesy, such as a pen or medical textbook.”

Doctors echo this view. Many are insulted by the suggestion that drug-company gifts influence their prescribing practices. A letter to the editor by Dr. Patrick Sweeney explains:

I still consider medicine to be the noblest of professions and those who enter it to be individuals of high ethical and moral character. They are the best and brightest who studied long and hard to be at the top of their college classes so that they could get into medical school, where they studied harder to be competitive candidates for residency programs. They graduated with $100,000 in educational debts, then put their personal lives and earning potential on hold for three to five more years during residency. To imply that such professionals could be “bribed” with a $4 mug into prescribing a medication that will cost their patients three to four times that of an equally effective cheaper alternative is demeaning and insulting to the majority of physicians who place the interest of their patients first and who practice cost-conscious medicine. Frankly it is offensive to think that physicians can be so

349. Id. at 92.
350. Id.
352. Id. at 1.
354. NAT’L ASS’N OF ATTORNEYS GEN., supra note 41, at 38.
355. See KASSIRER, supra note 126, at 63–67.
easily duped.356

But critics of drug-company gifts are not accusing the doctors of being corrupt, but of being human. Social science research establishes that the very human trait of reciprocation is deeply engrained.357 This research suggests that drug company gifts may exert a powerful—though unconscious—influence on physician prescribing behavior.358 Even small gifts "may be surprisingly influential."359 In 2000, the Journal of the American Medical Association published a review of the literature on the subject, which found relationships with drug representatives resulted in "nonrational" prescribing, rapid adoption of new drugs, decreased prescription of generics, and higher prescription costs.360 After enjoying drug-company hosted meals, doctors were more likely to ask for that company’s drugs to be added to their practice formularies.361 In its position paper on the subject, the American College of Physicians noted that the "gift relationship" creates a sense of obligation.362 As it concluded:

[T]he prevailing purpose of the gift is to establish the identity of the donor in the mind of the recipient and to oblige the recipient to reciprocate... The acceptance of even small gifts can affect clinical judgment and heighten the perceptions (as well as the reality) of a
Yet, doctors ""are generally unaware of the bias, so they do not make efforts to correct for it."" In one study, fewer than half of the faculty surveyed thought that they were influenced by free samples, subsidized education, meals, and gifts. Ironically, although most physicians deny that they are influenced by marketing efforts, they believe their colleagues are influenced by the same efforts. As one observer noted, ""Evidence is steadily mounting that we physicians are, in fact, influenced by the industry's largess. The proof does not by itself matter. What matters is how blind we are to the fact that we are being influenced."" And a study reported in the Journal of the American Medical Association documented a three-fold increase in the use of a particular drug following one company's marketing campaign. Another study concluded that while doctors reported relying on scientific literature to make prescribing decisions and discounted the influence of detailers and drug marketing, in fact they predominately relied on commercial information. ""The professional blindness to the influence of even small gifts is not a quibble about trivial trinkets. A thorough review of the literature on gifting concluded that "“most studies found negative outcomes associated with the interaction.'"

The marketing influences on prescribing decisions have adverse consequences for both the individual patient and for our health care system. For the individual patient, the aggressive promotion of prescription drugs presents three main problems. First, if the use is off-label, the drug may be ineffective or downright detrimental in treating the medical condition, and there is usually no scientific evidence to support the off-label use. Second, the increasing reliance on drug

363. Id.
364. AM. COLL. OF EMERGENCY PHYSICIANS, supra note 332 (quoting Dana & Loewenstein, supra note 358, at 252).
365. KASSIRER, supra note 126, at 63.
366. Greider, supra note 37, at 72; KASSIRER, supra note 126, at 72; AM. COLL. OF EMERGENCY PHYSICIANS, supra note 332 (citing W. P. McKinney et al., Attitudes of Internal Medicine Faculty and Residents Toward Professional Interaction with Pharmaceutical Sales Representatives, 264 JAMA 1693, 1693-97 (1990)).
368. Michael E. Dieperink & Lisa Drogemuller, Industry-Sponsored Grand Rounds and Prescribing Behavior, 285 JAMA 1443, 1443-46 (2001); accord Angee, supra note 7, at 141 (stating that doctors generally prescribe more of the sponsor's drugs after attending a continuing medical education meeting provided by the sponsor).
369. See Jerry Avorn et al., Scientific Versus Commercial Sources of Influence on the Prescribing Behavior of Physicians, 73 AM. J. MED. 4, 4-8 (1982).
370. Wazana, supra note 36, at 378.
371. See Radley et al., supra note 10, at 1021.
therapies creates the danger of overmedication and drug interactions. And finally, the heavily promoted drug is sure to be more expensive than an off-patent treatment or a generic drug. From a public health perspective, this escalating expense burdens our entire health care system. The ripple effect of these individual prescribing decisions has become a tidal wave. According to a report by the National Association of Attorneys General, the single biggest factor driving the increase in healthcare costs is the price of prescription drugs. Experts estimate that the off-label market ranges from 20% to 60% of the nation's $235 million prescription drug bill.

The problem is reflected in Medicaid's policy for covering off-label prescriptions. In 1997, Congress named Drugdex Information Service as one of the three organizations that determine whether off-label uses will be covered by Medicaid. Drugdex is a large firm that includes medical education and communication companies. These MECCs conduct flimsy Phase IV research and present CME courses on off-label uses which end up being listed on the Drugdex list. Given this arrangement, one might expect Drugdex to list a large number of off-label uses, and it does—twice as many as the other two approved directories which are nonprofit. According to Drugdex, Neurontin—the example used above to illustrate overly-aggressive off-label promotion—can be prescribed for "hiccups, nicotine withdrawal, migraine, and just about anything else you care to name, and Medicaid has to pay for it." And, of course, none of these uses were ever subject to FDA scrutiny. In other words, taxpayers end up paying for expensive prescription drugs that have never been proven safe or effective for treatment of the conditions for which they are prescribed. And the financial consequences are sure to escalate.

372. See Angell, supra note 7, at 169–72.
373. An example provided by letter to the Journal of the American Medical Association illustrates the point. E. Haavi Moreim, Prescribing Under the Influence, Markkula Ctr. for Applied Ethics (Santa Clara Univ.), http://www.scu.edu/ethics/publications/submitted/morreim/prescribing.html (last visited Apr. 1, 2007). A patient with an infected insect bite was initially prescribed penicillin, the preferred drug for minor infections. Id. But the intern's prescription was overruled by the resident who prescribed a new antibiotic costing $183 a day. Id. The attending physician looked into the matter and found the resident had just been entertained by the drug representative of the company that made the new drug. Id. This anecdote is borne out by the studies documenting the effectiveness of company promotions where the touted benefits are not supported by the scientific literature.
374. See Angell, supra note 7, at xiii.
375. Nat'l Ass'n of Attorneys Gen., supra note 41, at 7; accord Angell, supra note 7, at xii.
377. Angell, supra note 7, at 204.
378. Id. at 204–05.
379. See id. at 205.
380. Id.
381. See supra Part I.B.1.
382. Angell, supra note 7, at 205.
383. See id. at 206.
since the recently enacted Medicare prescription drug benefit will cover a number of off-label uses.\textsuperscript{384}

The pharmaceutical industry has argued in favor of relaxed regulation of drug marketing on the grounds that drug companies disseminate valuable information about the latest pharmaceutical advances to busy doctors who would otherwise fail to provide their patients with the best available treatment.\textsuperscript{385} But the information provided by drug companies is not a valuable resource for busy doctors because it is biased and unreliable. Biased sources are actually "distracting [doctors] from getting objective information and encouraging them to prescribe unapproved, unnecessary, and unnecessarily expensive medications."\textsuperscript{386}

Health care professionals are increasingly aware of the problem of marketing affecting prescribing decisions. The American College of Emergency Physicians has recognized that "such promotional [activity] has been proven to influence medical decision-making, and studies have found decision makers unable to recognize its impact."\textsuperscript{387} The American College of Physicians-American Society of Internal Medicine's Ethics and Human Rights Committee adopted a position providing that accepting "gifts, hospitality, trips and subsidies of all types from industry . . . is strongly discouraged. Physicians should not accept gifts, hospitality, services, and subsidies from industry if acceptance might diminish, or appear to others to diminish, the objectivity of professional judgment."\textsuperscript{388} The members of the American Medical Student Association adopted a PharmFree campaign seeking an end to gift giving, free lunches, sponsored education, and paid speaking.\textsuperscript{389} More than 5000 students have taken the pledge to accept no money, gifts, or hospitality from the drug industry and not to rely on information from drug detailers.\textsuperscript{390}

To fulfill their professional obligations to their patients, doctors need a reliable "evidence-based analysis of the relative clinical effectiveness of prescription drugs."\textsuperscript{391} Evidence-based medicine is the

\textsuperscript{384} Moyer, supra note 6, at 927.
\textsuperscript{386} Kassirer, supra note 126, at 85.
\textsuperscript{389} Jim Ritter, Medical Students Just Saying No to Drug Company Gifts: Movement Growing to Reject Overtures from Pharmaceutical Reps, CHI. SUN TIMES, Mar. 30, 2006, at 20.
\textsuperscript{390} Id.
\textsuperscript{391} NAT'L ASS'N OF ATTORNEYS GEN., supra note 41, at 77.
systematic analysis of results of controlled trials. If rigorous criteria are applied, the recommendations provided by this research are objective and highly reliable. Fortunately, some recent initiatives may provide the needed alternative to doctors' misplaced reliance on drug-company marketing to make prescribing decisions.

Specifically, the FDA has launched a website called Drug Watch, which discloses risk information about off-label prescriptions. On the state level, the proceeds from the Neurontin settlement are funding grants to improve prescribing by educating health care professionals about drug company marketing and sources of impartial and balanced information about drugs. As Dr. Linda Pinsky of the University of Washington's new program explained, drug companies spend more than $12 billion annually on marketing in the United States, which is more than is spent on medical education nationally. The industry knows the effects of this advertising. According to Dr. Pinsky, "[T]he CEOs of these businesses are neither philanthropists nor stupid. The pharmaceutical industry conducted outcome studies on their advertising campaigns long before they did on their medications."

The Center for Evidence-Based Policy at the Oregon Health and Science University is developing a comprehensive database for evidence-based medicine. The Center has combined a coalition of thirteen states and two other organizations to evaluate "the relative clinical effectiveness of [twenty-five] major classes of prescription drugs." This approach offers the hope both of controlling unnecessary spending on expensive new prescription drugs which are no more effective than the older and cheaper generics, and also of protecting patients from adverse health effects. For example, the Oregon Center identified cardiac problems associated with Vioxx in 2001, reported these risks to the

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392. KASSIRER, supra note 126, at 82; see Oates, supra note 37, at 1273–74 (explaining how the absence of reliable research on off-labels uses "frustrates the effective practice of evidence-based medicine").

393. KASSIRER, supra note 126, at 82.


397. Id.

398. See NAT’L ASS’N OF ATTORNEYS GEN., supra note 41, at 77.

399. Id.
public, and discouraged its purchase by Medicaid.\textsuperscript{400} Vioxx was not withdrawn from the market for these risks until 2004.\textsuperscript{401} Similarly, the Dartmouth College Project is creating "Prescription Drug Fact Boxes" providing evidence-based information quickly—similar to the format of nutrition labeling for food—for doctors to use when prescribing drugs.\textsuperscript{402}

States are beginning to use this evaluative process in compiling their formularies or Preferred Drug Lists (PDLs). In the Medicaid program, PDLs are adopted to provide which drugs may be prescribed without seeking a prior authorization.\textsuperscript{403} As of 2004, twenty-seven states had adopted PDLs.\textsuperscript{404} The listed drugs are most frequently prescribed by doctors.\textsuperscript{405} To get on the PDL, drug companies offer better discounts to the states in addition to those required by federal law.\textsuperscript{406} In addition to enabling states to negotiate better discounts,\textsuperscript{407} PDLs can become an objective source of information for prescribers. For example, in 2002, Oregon adopted an evidence-based PDL.\textsuperscript{408} While cost is a factor in the decision to include a drug on the PDL, it is the last factor.\textsuperscript{409} Similarly, in 2002, Michigan implemented a PDL based on clinical evaluations to determine the best drugs in forty-four drug classes.\textsuperscript{410} The benefits of this plan were immediate: a savings of $45 million for the first year for 330,000 participants.\textsuperscript{411}

Information about relative cost is also becoming more accessible. Attorneys General are creating pharmaceutical price websites to enable consumers to compare retail prices.\textsuperscript{412} These websites enable doctors and patients to comparison shop for prescription drugs.\textsuperscript{413} The range can be significant. In Maryland, in April 2004, for example, prices varied more than $100 for a thirty-day supply of a single drug.\textsuperscript{414} Similarly, a recent survey in New York found that the price of a commonly-prescribed, cholesterol-lowering drug, Zocor, was $96 at one pharmacy and $190 at another only four miles away.\textsuperscript{415} Vermont has adopted a Detailing

\textsuperscript{400} Id. at 79.
\textsuperscript{401} Press Release, Merck & Co., Inc., supra note 74.
\textsuperscript{403} Nat'l Ass'n of Attorneys Gen., supra note 41, at 83.
\textsuperscript{404} Id. at 84.
\textsuperscript{405} Id. at 83.
\textsuperscript{406} See id.
\textsuperscript{407} Id. at 84.
\textsuperscript{408} Id.
\textsuperscript{409} Id.
\textsuperscript{410} Id.
\textsuperscript{411} Id. at 85.
\textsuperscript{412} Id. at 94.
\textsuperscript{413} See id.
\textsuperscript{414} Id.
\textsuperscript{415} Id.
Disclosure Law which requires drug marketers to disclose to doctors and other prescribers the prices of the drugs they market as well as the prices of other drugs in the same therapeutic class.\textsuperscript{416}

These initiatives provide unbiased, evidence-based information to doctors to offset the biased and exaggerated claims of the drug companies. But the reality is that pharmaceutical marketing is growing, not shrinking, and that doctors rely on drug company promotional materials in making prescribing decisions. Unfortunately, many doctors are unaware of marketing's influence on their prescribing decisions, deny that it has any effect, and mistakenly report that they rely on scholarly articles rather than promotional materials in making prescribing decisions. And, of course, patients have no idea of the pervasive drug-company influence.

II. EXPANDING THE DOCTRINE OF INFORMED CONSENT TO REQUIRE DISCLOSURE OF OFF-LABEL PRESCRIPTIONS AND CONFLICTS OF INTEREST

As the preceding Part explains, off-label prescribing of drugs which have not been proven safe or effective for the prescribed use drives up the cost of health care and exposes patients to unnecessary risks. Aggressive drug marketing results in the prescription of expensive new drugs when older ones are equally effective, less expensive, and less risky. Moreover, industry marketing creates conflicts of interest for doctors. I propose that the tort doctrine of informed consent be expanded to require doctors to disclose off-label uses and conflicts of interest created by drug-company marketing. This Part describes the evolution of the doctrine of informed consent and then analyzes the proposed expansion of the doctrine.

A. EVOLUTION OF THE DOCTRINE OF INFORMED CONSENT

The doctrine of informed consent reflects the value we place on patient autonomy. Until the early twentieth century, doctors were not required to inform their patients of the risks of and alternatives to a prescribed treatment.\textsuperscript{417} The law assumed that doctors knew best and that patients were sufficiently protected by their doctors' interest in their well-being.\textsuperscript{418} The doctrine of informed consent—now adopted in all fifty states—transformed this understanding and with it the doctor-patient relationship.\textsuperscript{419}

\textsuperscript{416} Id. at 92.
\textsuperscript{417} See Morris, supra note 37, at 317.
\textsuperscript{418} Id. at 313-17.
\textsuperscript{419} AARON D. TWERSKI & JAMES A. HENDERSON, JR., TORTS: CASES AND MATERIALS 78 (2003); Morris, supra note 37, at 315. Despite this widespread acceptance, the doctrine has its critics. See id. at 315-16; Peter H. Schuck, Rethinking Informed Consent, 103 YALE L.J. 889, 904-06 (1994); Aaron
In the beginning, the patient’s claim for lack of consent was framed as a battery action. Battery arises where the plaintiff is touched without consent. In the earliest cases, the patient had either refused surgery or consented to a different procedure than the one the surgeon actually performed, so battery fit the facts. As Justice Cardozo explained, “Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient’s consent commits an assault, for which he is liable in damages.” For example, in one early case, the plaintiff successfully alleged a battery cause of action when she consented to surgery on one ear, but the surgeon operated on her other ear.

Over time, as patients asserted greater autonomy rights, the doctrine of informed consent evolved as a negligence theory. As the Kansas Supreme Court declared in 1960, “Anglo-American law starts with the premise of thorough-going self determination” which imposes on doctors the duty to make “those disclosures which a reasonable medical practitioner would make under the same or similar circumstances.” Today, the medical profession adopts this informed patient approach as the appropriate standard of care. Under this approach—as in other medical malpractice cases—negligence is determined by whether the doctor conformed to the standard of care of other physicians in good standing. This medical-custom standard is followed in a slight majority of states, many under statutory authority.


421. Noah, supra note 120, at 364.

422. Morris, supra note 37, at 318–19.


424. Mohr v. Williams, 104 N.W. 12, 15–16 (Minn. 1905).

425. Noah, supra note 120, at 364; see also Morris, supra note 37, at 319, 323; Prillaman, supra note 420, at 44.


427. The policies of both the American Medical Association (AMA) and the American Hospital Association (AHA) recognize that good medical practice requires the physician to keep the patient informed. Robert John Kane, *Information Is the Key to Patient Empowerment*, 11 ANNALS HEALTH L. 25, 29 (2002).

428. Natanson, 350 P.2d at 1106, discussed in Morris, supra note 37, at 326; Prillaman, supra note 420, at 45.

But many courts have rejected the medical-custom standard as undermining the very notion of patient autonomy and self-determination that informed consent is designed to protect. In a landmark decision, Canterbury v. Spence, the court refocused the analysis on the information the patient would need to make an informed decision rather than on the information a doctor would customarily disclose. As the court explained, the doctor must disclose the "material risks" which a reasonable patient would consider significant. In adopting this approach, the California Supreme Court explained that self-determination requires the patient, not the doctor, to set the standard since her right to weigh her subjective fears against the disclosed risks is a personal matter, not a medical question, and must be "reserved to the patient alone.

The obligation to obtain the patient's informed consent dovetails with the learned intermediary doctrine. Under the learned intermediary rule, doctors, not drug companies, are responsible for informing patients of the risks of prescription drugs. The rule reflects the courts' view that warnings from drug companies would not be feasible and would interfere with the doctor-patient relationship. The rationale is that only medical professionals have the required knowledge, training, and judgment to determine which drugs would be the best treatment for individual patients. While critics have argued that doctors fail to pass on sufficient information about drugs, the doctrine has been adopted in almost every state.

430. See Noah, supra note 120, at 367.
431. 464 F.2d 772 (D.C. Cir. 1972), discussed in Morris, supra note 37, at 328–29.
433. Canterbury, 464 F.2d at 787. This reasonable patient standard has been criticized as undermining individual patient autonomy, and some courts have adopted a subjective standard for each particular patient. See, e.g., Scott v. Bradford, 606 P.2d 554 (Okla. 1980); accord Morris, supra note 37, at 329–30.
435. Dobbs, supra note 429, at 1010; David G. Owen, Products Liability Law 608 (2005); Restatement (Third) of Products Liability § 6(d) (1998); Frank C. Woodside, III, & Margaret M. Maggio, The Learned Intermediary Doctrine: Is It Eroding?, Mealey's Emerging Drugs & Devices, Apr. 21, 2005, at 21. A companion theory that can be advanced in off-label cases is that the drug company's insulation from products liability actions is defeated where it overpromoted the drug and downplayed the risks. Owen, supra, at 615 n.79.
436. Dobbs, supra note 429, at 1011.
439. Owen, supra note 435, at 609.
Courts have recognized an exception to the requirement of informed consent when the knowledge of the risk would harm the patient. As one court explained, this therapeutic exception is necessary since the doctor’s primary duty is to do what is best for the patient. “[W]here full disclosure would be detrimental to a patient’s total care and best interests a physician may withhold such disclosure, for example, where disclosure would alarm an emotionally upset or apprehensive patient.”

In the United States today, this is generally where the law stands. A slight majority of states continue to apply the reasonable-doctor standard, with the Canterbury reasonable-patient standard as the minority alternative. As scholars have observed, “The law of informed consent has undergone little analytic development since Canterbury.” Under the learned intermediary rule, doctors are responsible for informing patients of the risks of drug therapies. Finally, the therapeutic exception relieves doctors of the duty to disclose risks and alternatives when disclosure would be detrimental to patient care.

A few jurisdictions have expanded the doctrine to require doctors to disclose other relevant information. For example, a few cases require the doctor to disclose risks related to the doctor’s health or inexperience. A handful of cases have required the disclosure of other facts that would affect the patient’s decision. Specifically, a few cases have required the doctor to disclose that a prescribed treatment is experimental and that

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440. Dobbs, supra note 429, at 656.
442. Scott, 606 P.2d at 558; accord Beck & Azari, supra note 2, at 86.
443. Dobbs, supra note 429, at 655; Noah, supra note 120, at 376.
445. See supra notes 435–39 and accompanying text.
446. See supra notes 440–42 and accompanying text.
447. Hidding v. Williams, 578 So. 2d 1192, 1198 (La. Ct. App. 1991) (affirming a judgment against a doctor who failed to disclose his chronic alcohol abuse); Faya v. Almaraz, 620 A.2d 327, 333 (Md. 1993) (holding that a complaint alleging doctor failed to disclose his HIV-positive status should not have been dismissed). But see K.A.C. v. Benson, 527 N.W.2d 553, 561–62 (Minn. 1995) (holding that although the doctor was HIV-positive the complaint failed to state a cause of action where the patient was not actually exposed to the virus); Kaskie v. Wright, 589 A.2d 213, 216–17 (Pa. Super. Ct. 1991) (holding a doctor was not required to disclose his alcoholism).
448. Johnson v. Kokemoor, 545 N.W.2d 495, 505 (Wis. 1996) (holding a doctor was required to disclose his limited experience with an extremely difficult procedure). But see Duttry v. Patterson, 771 A.2d 1255, 1259 (Pa. 2001) (holding the duty of informed consent was limited to the risks inherent in the procedure and that the doctor was not liable for misrepresenting the number of times he had performed the surgery (he said sixty times when it was only nine)); Kaskie, 589 A.2d at 216–17 (holding that only information about the medical procedure is required to be disclosed); Whiteside v. Lukson, 947 P.2d 1263, 1264–65 (Wash. Ct. App. 1997) (holding that a surgeon was not required to disclose that he had never performed the surgery before and had only attended a two-day class on it where it was demonstrated on pigs).
HASTINGS LAW JOURNAL

the doctor has a financial interest that might affect the exercise of professional judgment. For example, in Moore v. Regents of the University of California, the California Supreme Court held that doctors had a duty to disclose their research interest in developing a cell line from the patient’s spleen cells and their financial interest in patenting this cell line. As the next section will explain, in my view, this last line of cases should be expanded to require doctors to disclose off-label prescriptions and conflicts of interest resulting from drug-company marketing.

B. EXTENSION OF THE DOCTRINE OF INFORMED CONSENT TO REQUIRE DISCLOSURE OF OFF-LABEL PRESCRIPTIONS AND CONFLICTS OF INTEREST

As we have seen, the doctrine of informed consent promotes patient autonomy in medical decision-making. Under the reasonable-patient approach, doctors must disclose information that would be material to the patient’s decision to consent to a recommended course of treatment, including risks from drug therapies. The question thus becomes whether off-label uses and drug-company influences are material to a patient’s consent to treatment. In my view, both are material. Since off-label uses have not been proven safe and effective under FDA standards and since most are not supported by scientific evidence, they may carry uncertainties and risks that the patient would not accept. And, in deciding whether to accept the risks of any drug—especially an off-label drug—the patient would want to know whether drug-company marketing

1978) (requiring disclosure that treatment was considered investigational by the FDA); Moore v. Regents of Univ. of Cal., 793 P.2d 479, 484 (Cal. 1989) (referring to CAL. HEALTH & SAFETY CODE § 24173(c) (West 2006)) (requiring the physician to disclose that the physician is conducting a medical experiment on a patient); Retkwa v. Orentreich, 584 N.Y.S.2d 710, 713 (1992) (requiring disclosure that liquid silicone injections were not FDA approved); Estrada v. Jaques, 321 S.E.2d 240, 254–55 (N.C. Ct. App. 1984) (requiring disclosure that surgical procedure was experimental).

450. Moore, 793 P.2d 479, 483–84 (Cal. 1990) (referring to CAL. BUS. & PROF. CODE § 654.2 prohibiting a physician from referring a patient to an organization in which the physician has a significant beneficial interest without a prior written disclosure of that interest); Shea v. Esensten, 622 N.W.2d 130, 135 (Minn. Ct. App. 2001) (holding a doctor could be held liable for failing to disclose HMO restrictions on expert referrals under ERISA regulations for fiduciary duties); D.A.B. v. Brown, 570 N.W.2d 168, 171–72 (Minn. Ct. App. 1997) (holding a physician who received illegal kickbacks from a drug company for prescribing a growth hormone could be liable for medical malpractice but finding that the claim failed based on the lack of injury and failure to file within the statute of limitations). But see Corrigan, 874 F. Supp. at 659 (holding a patient is entitled to be informed of surgical risks, but not of a doctor’s financial interest in a company which manufactured a medical device); Neade v. Portes, 739 N.E.2d 496, 505–06 (Ill. 2000) (declining to recognize a cause of action where a doctor failed to disclose HMO incentives to discourage expert referrals).

451. Moore, 793 P.2d at 483–85. But see Corrigan, 874 F. Supp. at 657, 659 (holding a patient is entitled to be informed of surgical risks, but not of a doctor’s financial interest in a company which manufactured a medical device).

452. Radley et al., supra note 10, at 1021.
may have influenced the doctor’s prescribing decision.453

I. Duty to Disclose Off-Label Prescriptions

Patients believe that their prescriptions are for FDA-approved uses.454 Off-label uses are not supported by the extensive research and rigorous scrutiny that is required for FDA approval, and most off-label uses are not supported by scientific evidence.455 When a drug is prescribed off-label, it has not necessarily been proven effective at all in treating the patient’s condition456 and has certainly not been proven more effective than older, approved drugs.457 Indeed, the off-label use may be detrimental.458 In short, the patient thinks the drug has been proven safe and effective for the prescribed treatment following rigorous scrutiny by the FDA, but with off-label uses it has not.

Is the fact of off-label use material to the patient’s decision? Well, it certainly ought to be. Basically, the doctor may not know whether it will help or harm the patient. If an FDA-approved drug is available, most patients would undoubtedly prefer the thoroughly-tested drug that has been proven safe and effective to the untested, potentially dangerous, off-label alternative. And if an approved generic is available, most patients would undoubtedly prefer the well-tested, safe, effective, and cheaper generic. Moreover, even for FDA-approved uses, some risks are discovered later. For example, the unexpected cardiovascular risks of Cox2 drugs including Vioxx were not known until they were widely prescribed to a large patient population.459 The longer a drug is in use, the more is known about its potential risks.460 So it is generally safer to take the older, approved drug with an established history than the newer, off-label drug where additional risks may yet be discovered.461

Surprisingly, given the frequency of off-label prescribing and the attendant risks, research has disclosed no case holding that the doctrine of informed consent requires a doctor to disclose that a prescription is off label.462 Indeed, only a handful of cases have considered the question. In

453. While the research on patients’ attitudes toward drug company marketing is limited, it suggests that “patients are more likely than doctors to believe that gifts may influence prescribing behavior and that patients tend to view gifts that influence prescribing behavior as inappropriate.” Blumenthal, supra note 131, at 1888.
454. HARRIS POLL, supra note 4, at 1; Tansey, supra note 4.
455. Radley et al., supra note 10, at 1021.
456. Id.
457. GREIDER, supra note 37, at 98.
458. Radley et al., supra note 10, at 1021.
460. GREIDER, supra note 37, at 98.
461. See id.
462. A few cases have held that the off-label status of a prescription is relevant under a general negligence theory if the defendant doctor has been careless, imprudent or unprofessional. See Richardson v. Miller, 44 S.W.3d 1, 15 (Tenn. Ct. App. 2000). One case, not officially reported, found that failure to disclose risks associated with off-label use created a question of fact on informed
several cases involving pedicle screws, the courts have concluded that off-label use was not a required disclosure.\textsuperscript{465} In these cases, the bone screws were approved for long and flat bones like leg and arm bones and then were used off-label in spinal fusion operations.\textsuperscript{463} The courts concluded that the lack of FDA approval was not necessarily material to the patient's decision to undergo surgery.\textsuperscript{465} As one court explained, FDA classifications "do not speak directly to the medical issues surrounding the particular surgery."

This view reflects the position of the authors of the only article examining the issue.\textsuperscript{467} In their view, FDA-approval is outside the doctrine of informed consent since it is medically irrelevant to medical risk.\textsuperscript{468} They also argue that disclosure would unduly frighten patients who would equate the lack of FDA approval with FDA disapproval and lead them to refuse optimal treatments.\textsuperscript{469} And finally, they argue that

\textsuperscript{463} In re Orthopedic Bone Screw Prod. Liab. Litig., No. 1014, 9408-0002, 1996 WL 107556, at *5 (E.D. Pa. Mar. 8, 1996) [hereinafter Bone Screw Litigation] (holding that disclosure was not required because FDA labels for a medical device do not speak directly to the medical issues); Alvarez v. Smith 714 So. 2d 652, 654–55 (Fla. Dist. Ct. App. 1998) (holding that disclosure was not required because FDA status of bone screws was not a medical risk); Blazoski v. Cook, 787 A.2d 910, 922 (N.J. Super. Ct. App. Div. 2002) (holding that disclosure of FDA labeling of bone screws as a class III device was not required because FDA status did not purport to weigh in on medical judgment); Sita v. Long Island Jewish-Hillside Med. Ctr., 22 A.D.3d 743, 743–44 (N.Y. App. Div. 2005) (holding that medical center was not required to disclose FDA regulatory status of bone screws); Klein v. Biscup, 673 N.E.2d 225, 231 (Ohio Ct. App. 1996) (holding that disclosure was not required because the off-label use of screws was not itself a material risk, and because the FDA does not regulate the practice of medicine); Southard v. Temple Univ. Hosp., 781 A.2d 101, 106–08 (Pa. 2001) (holding that disclosure was not required because FDA labeling of bone screws as a class III device was merely administrative, and did not constitute a material fact or risk in the surgical procedure); Piazza v. Myers, 37 Pa. D. & C.4th 322, 325–26 (Pa. Ct. Com. Pl. 1997), available at 1997 WL 1133693, *2 (holding that FDA status of a device was not a proper subject matter for an informed consent claim); see also Beck & Azari, supra note 2, at 72 (arguing that "off-label" reflects legal status, not a medical fact); C. Murray Harris, Informed Consent: Physicians Need Not Inform Patients of the FDA Classification of a Medical Device—Southard v. Temple University Hospital, 27 Am. J.L. & MED. 489, 490–91 (2001) (discussing the Southard decision and its impact on medical practice). See generally 21 U.S.C. § 360c(a)(1)(C) (2002) (definition of a class III device).

\textsuperscript{464} Bone Screw Litigation, 1996 WL 107556, at *1.

\textsuperscript{465} Id. at *5; Alvarez, 714 So. 2d at 654; Blazoski, 787 A.2d at 918; Klein, 673 N.E.2d at 231; Southard, 781 A.2d at 107.

\textsuperscript{466} Southard, 781 A.2d at 107.

\textsuperscript{467} Beck & Azari, supra note 2. This article has been repeatedly cited by the courts considering prescriptions for off-label use. Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 350 (2001); In re Orthopedic Bone Screw Prod. Liab. Litig., 159 F.3d 817, 829 (3d Cir. 1998); Alvarez, 714 So. 2d at 654; Blazoski, 787 A.2d at 919; Southard, 781 A.2d at 104; Richardson, 44 S.W.3d at 9.

\textsuperscript{468} Beck & Azari, supra note 2, at 72.

\textsuperscript{469} Id. at 85.
requiring disclosure would impose an undue burden on doctors whose attention would be diverted from medical literature to legalistic FDA administrative regulations.470

In my view, these concerns fail to overcome the policy of patient autonomy and self-determination embodied in the doctrine of informed consent. First, with respect to relevance, the fact that a drug has not been proven safe and effective for a particular treatment under the rigorous FDA standards is certainly relevant to the decision of whether to take the drug. Lack of approval does not necessarily mean that the drug is dangerous or ineffective, but it should raise a concern about safety that the patient should weigh in deciding whether to consent to the treatment since it has not been proven safe and effective for the prescribed purpose. Since most off-label uses are not supported by scientific evidence, they may be ineffective or even detrimental.471 At the very least a patient should be informed as to whether there is an FDA-approved alternative and why the doctor is recommending the off-label use instead.

Second, as to undue patient fear, the doctor can educate the patient about off-label uses in the informed-consent conversation. The notion that patients cannot make competent health-care decisions when provided truthful information flies in the face of the values supporting the doctrine of informed consent. This argument reflects the outdated, paternalistic view that patients are like timid children who cannot be trusted to make intelligent decisions about their own health care. Moreover, in the exceptional case where disclosure would be detrimental to the patient’s health, the therapeutic exception to the informed consent requirement already allows a doctor to withhold the information.472 Rather than routinely withholding this information from perfectly competent patients, doctors should disclose it to further the policy of patient autonomy underlying the doctrine of informed consent.

Moreover, the argument that off-label disclosure will discourage overly timid patients from electing the best course of treatment assumes that the off-label use actually is the best course of treatment. But that assumption is dubious because off-label uses are often unproven either as to safety or efficacy.473 Compared to an FDA-approved treatment, the off-label use may be more effective, equally effective, less effective, totally ineffective, or actually detrimental. In many cases, the doctor simply doesn’t know. As Dr. Arnold Relman, a former editor of the New England Journal of Medicine observed, “You’re taking a medicine

470. Id. at 100-01.
471. Radley et al., supra note 10, at 1021, 1026.
472. See supra notes 440-42 and accompanying text.
473. See Radley et al., supra note 10, at 1021, 1026.
because a company needs to market it. Who knows if it will work? While some believe that patients will be overly reluctant to consent to off-label uses, the truth may well be that doctors are overly confident in prescribing them. The doctor’s confidence in an off-label use may have been induced by exaggerated drug-company claims based on unreliable research delivered over a gourmet dinner that clouds the doctor’s judgment with an unconscious desire to reciprocate. The patient’s caution may be the needed antidote to the doctor’s unwarranted reliance on drug-company marketing. In any event, under the doctrine of informed consent, it should be the patient’s choice.

Finally, determining FDA status is far from an onerous burden. The information about FDA approval is readily available in the approved PPI, the PDR, and on-line services. In fact, the FDA has recently taken additional steps to make this information readily available to doctors. As of June 2006, the FDA will require drug manufacturers to provide the FDA-approved uses and side effects of their prescription drugs in a computer format that will be readily accessible to doctors’ computers and hand-held devices. In addition, the FDA is standardizing and simplifying the approval information to make it more readily available and understandable. And, the FDA is currently issuing alerts to patients and doctors on its website.

Medical literature supports the feasibility of disclosing off-label uses. Specifically, in 2006, a multidisciplinary group developed a policy for off-label prescribing for medical centers. It concluded that for innovative off-label uses where the prescribing is reasonable but not sufficiently tested to allay concerns about safety, efficacy, and cost-effectiveness, “physicians... must meet their ethical obligations by ensuring that the patient is informed and provides consent prior to administering the drug.” Indeed, one insurance company has disseminated a standard.

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475. See Radley et al., supra note 10, at 1021 (finding that most off-label uses were not supported by substantial scientific evidence).

476. See supra notes 161–68 and accompanying text.

477. See supra notes 81–82 and accompanying text.

478. See supra note 83 and accompanying text.

479. See supra note 394 and accompanying text.


481. Id. at 3922.

482. See supra note 394 and accompanying text.


484. Id. at 259; accord Jan M. Keltz, Off-Label Use of Prescription Medication: Nursing Implications, 30 Nephrology Nursing J. 99, 99 (2003) ("From a liability standpoint, patients should be
form for doctors to obtain informed consent to off-label uses. Thus, rather than being unfeasibly burdensome, off-label disclosure is the recommended medical practice.

A few hypotheticals illustrate how the proposed expansion of informed consent is likely to operate. First, assume a patient suffers from chronic back pain. Several alternative treatments are available, including generics that have been FDA-approved for back pain and new, on-patent drugs that have not. Most patients would undoubtedly elect a generic drug that has been proven safe and effective for back pain rather than an epilepsy drug that has never been approved for pain management. Moreover, the generic will be much cheaper than the off-label, on-patent alternative. Under these circumstances, the patient should be informed of the alternatives and given the choice. If the generic proves ineffective, the patient can always reconsider her choice.

Second, assume a patient is dying of cancer. There are no FDA-approved drugs to treat her advanced condition, and scant reliable research on off-label alternatives. Some patients will be willing to try the off-label therapies, and some will not. As explained by FDA Commissioner Jane E. Henney, "We all recognize that most patients faced with grave diseases are willing to assume greater risks." But some patients will be more risk-averse, preferring to focus on the quality of their remaining time rather than undergoing risky treatments with unstudied and potentially debilitating side effects. Again, under these circumstances, the patient should be given the information necessary to make this profoundly personal decision.

Third, assume an irrational, emotionally-overwrought patient with a serious medical condition would be likely to reject an off-label prescription despite extensive, reliable research showing that it is by far the best treatment and poses few risks. In this case, the therapeutic exception would apply. As explained briefly above, since the doctor's ultimate responsibility is to do what is best for the patient, where disclosure would be detrimental to the patient's care, disclosure is not required. In short, in each of these cases, applying the doctrine of

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informed that a drug being prescribed is for an unlabeled use and informed of the rationale for the suggested treatment.

485. Abel Torres, The Use of Food and Drug Administration-Approved Medications for Unlabeled (Off-Label) Uses, 130 Archives Dermatology 32, 35-36 (1994) ("Although no specific informed consent appears to be required, unlabeled drug use best serves the patient and protects the physician from liability when it is accompanied by informed consent that adequately informs the patient of the innovative nature of the therapy together with the greater uncertainty of risk.").

486. Henney, supra note 66.

487. See supra notes 440-42 and accompanying text.
informed consent—including the established therapeutic exception—would maximize patient autonomy without compromising patient care.

While there are no cases holding that a doctor is required to disclose that a use is off-label, a few courts have concluded that disclosure is required when the treatment had received no FDA approval at all and when the FDA still considered the drug "investigational."\(^{488}\) A drug is categorized as "investigational" after animal testing when the manufacturer begins clinical testing on humans.\(^{489}\) As one court explained:

> It is a reasonable assumption that most patients, confronted with a doctor's recommendation for injection of a foreign substance, presume that such substance has been the subject of official testing, consideration, and approval, and implicitly or explicitly rely on this presumption as part of the basis of their "consent" to the treatment.\(^{490}\)

In other words, according to the court, since patients presume that therapies have survived the rigorous FDA-approval process for safety and efficacy and since their consent is based on that presumption, doctors should disclose the lack of FDA approval so that patients can factor that uncertainty and potential risk into their decision.

In my view, the patient's presumption of official testing and approval is equally operative when drugs are prescribed off-label and consent to the treatment is given with that understanding. Patients believe a drug has been officially tested and approved for the treatment the doctor is recommending.\(^{491}\) If a doctor prescribes a drug to treat back pain, the patient thinks it has been approved to treat pain, not epilepsy or depression. Where a drug has received FDA approval for a treatment, the patient justifiably presumes that the FDA has found it safe and effective for that purpose. But when it is prescribed off-label, the patient mistakenly presumes it has survived the FDA approval process and has been found safe and effective for that purpose. Contrary to the patient's presumption, the drug or device has not been proven safe or effective for

\(^{488}\) See supra note 449 regarding investigational status; see also Ahern v. Veterans Admin., 537 F.2d 1098, 1100-02 (10th Cir. 1976) (holding that informed consent was required where a doctor learned about using an unusually high dose of radiation to treat cancer at a medical conference and used it in treating the patient without disclosing that it was a departure from standard treatment); Corrigan v. Methodist Hosp., 874 F. Supp. 657, 658 (E.D. Pa. 1995) (experimental status of bone screws held to be relevant to informed consent claim); Gaston v. Hunter, 588 P.2d 326, 350-51 (Ariz. Ct. App. 1978) (requiring disclosure that treatment was considered investigational by the FDA); Retkwa v. Orentreich, 584 N.Y.S.2d 710, 713 (N.Y. Sup. Ct. 1992) (holding that failure to disclose liquid silicone injections' FDA status was material and relevant to malpractice claim); Estrada v. Jaques, 321 S.E.2d 240, 254-55 (N.C. Ct. App. 1984) (requiring disclosure that surgical procedure was experimental).

\(^{489}\) See Henry, supra note 61, at 367.

\(^{490}\) Retkwa, 584 N.Y.S.2d at 712 n.6.

\(^{491}\) Tansey, supra note 4.
the prescribed use according to FDA standards of proof. To correct the patient’s misunderstanding about the government’s finding of safety and effectiveness, the off-label status should be disclosed. Since the FDA has not found it safe and effective for the purpose, patients surely would want to know the doctor’s basis for recommending an off-label treatment. As we have seen, with off-label uses, the doctor may be relying on flimsy, company-sponsored “research” presented by company-paid consultants at company-sponsored CME programs followed by a gourmet meal and a round of golf. Even worse, the doctor may be relying on little or no scientific evidence at all. Caution and skepticism are warranted and should generate doctor-patient discussions about treatment risks and alternatives.

2. Duty to Disclose Conflicts of Interest

Although doctors deny it, drug-company promotions influence prescribing decisions. Free CME programs directly result in increased prescribing. Moreover, drug companies’ financial relationships with doctors may have an even greater influence. Doctors who sign up for a company’s speakers’ bureau can make thousands of dollars promoting the company’s drugs. In many Phase IV trials, doctors receive bounties for prescribing the company’s drug to their patients. Many doctors are paid handsomely as consultants or advisors to the drug company. Doctors readily prescribe drugs which they receive as free samples. And even small gifts have been proven to affect prescribing decisions. This pervasive, drug-company influence on prescribing decisions is unknown to patients. While doctors may not be conscious of it, and often

492. See Radley et al., supra note 10, at 1021.
493. It could be argued that the patient’s mistaken belief that the drug has been found safe and effective by the FDA vitiates the patient’s consent to the off-label use. See RESTATEMENT (SECOND) OF TORTS § 892B(2) (1979) (providing that consent is ineffective if it is induced by a substantial mistake known to the defendant).
494. See supra notes 161–63 and accompanying text.
495. Radley, supra note 10, at 1023.
496. See supra notes 161–63 and accompanying text.
497. See supra notes 265–69 and accompanying text. One study found that doctors who accepted an all-expense paid trip to sponsored symposia believed that the programs would not influence their prescribing decision, but actually increased their prescriptions threefold for the promoted drugs over the two years following the event. Peter S. Kussin, Prescription for Trouble, DUKE MED. NEWS, Winter 2002, http://www.dukemednews.org/news/controversy.php?id=6285.
498. See supra note 292 and accompanying text. For example, Dr. Peter Gleason admitted that he received more than $100,000 last year alone for promoting a narcolepsy drug for depression and pain relief. Alex Berenson, Indictment of Doctor Tests Drug Marketing Rules, N.Y. TIMES, Jul. 22, 2006, at A1. He was indicted for conspiring with the drug manufacturer to recommend the drug for potentially dangerous uses. Id.
499. See supra notes 225–31 and accompanying text.
501. See supra notes 314–25 and accompanying text.
502. See supra notes 332–70 and accompanying text.
vehemently deny it, these influences present the appearance and often the reality of a conflict of interest.

The doctrine of informed consent should be expanded to require the disclosure of drug company influences that create conflicts of interest or the appearance of conflicts of interest. A few cases have already recognized the duty of a doctor to disclose conflicts of interest in analogous situations. Specifically, in Moore v. Regents of the University of California, the California Supreme Court held that doctors had a duty to disclose their research interest in developing a cell line from the patient’s spleen cells and their financial interest in patenting this cell line.503

In Moore, the patient visited the UCLA Medical Center after being diagnosed with hairy-cell leukemia.504 UCLA doctors recommended that his spleen be removed.505 Without informing the patient, the doctor also made arrangements to conduct research on the patient’s spleen to develop valuable commercial products.506 Following the surgery, the doctor required him to return repeatedly for follow-up care.507 Each time blood, bone, skin, marrow, and sperm samples were drawn.508 But the doctor never disclosed, and in fact denied, having any financial interest in research relating to the patient’s samples.509 The doctor used the patient’s cells to develop a patented cell line.510 Under an agreement negotiated with the Genetics Institute to develop the cell line, one doctor acquired 75,000 shares of common stock and became a paid consultant.511 The doctors and Regents also negotiated payments of more than $400,000.512

As the California Supreme Court concluded, the doctor had a financial and research interest which his fiduciary duty required him to disclose.513 Perhaps the splenectomy and follow-up care were all medically appropriate. But perhaps the doctor’s recommendations were tainted—even unconsciously—by his conflicting personal interests. As the court explained, the “patient would want to know whether the physician had an economic interest that might affect the physician’s professional judgment.”514 A patient should be free of any suspicion that the doctor’s judgment is swayed by a profit motive.515 The court drew an
analogy to statutes requiring doctors to disclose whether they had a financial interest in organizations, including laboratories, when making referrals for treatment.\textsuperscript{516} Moreover, as the court explained, in treating a patient in whom the doctor has a research interest, the doctor’s research interest may influence his or her medical judgment.\textsuperscript{517} As the court concluded:

The possibility that an interest extraneous to the patient’s health has affected the physician’s judgment is something that a reasonable patient would want to know in deciding whether to consent to a proposed course of treatment. It is material to the patient’s decision and, thus, a prerequisite to informed consent.\textsuperscript{518}

Turning to drug company marketing influences, the \textit{Moore} analysis applies. For example, consider the Phase IV trials where doctors are paid by drug companies to prescribe certain drugs. As in \textit{Moore}, patients would want to know if the doctor’s opportunity to gain financially is influencing the decision to prescribe a certain drug. Also as in \textit{Moore}, these doctors have both a research interest and a financial interest that might be affecting their judgment. The patient is entitled to know that the doctor’s decision to prescribe a particular drug might be influenced—perhaps unconsciously—by the $2000 the doctor will receive as a result of the prescription or the $20,000 the doctor will receive by enrolling ten patients. The same is true where doctors receive educational grants or earn substantial sums as drug company spokespersons and consultants. The patient should be given the information necessary to weigh whether the doctor’s prescribing decision has been influenced by the income she earns from expanding the drug’s market. And, more subtly, research establishes that free CME and even modest gifts influence prescribing decisions.\textsuperscript{519} If the drug company’s marketing is influencing prescribing decisions, that influence is clearly “extraneous to the patient’s health,” in the words of the \textit{Moore} court, and material to the patient’s decision.

As with disclosure of off-label prescribing, medical literature supports disclosure of financial relationships that might create conflicts of interest. For example, a 2005 advisory opinion on the Code of Ethics of the American Academy of Ophthalmology recognized that the potential for a conflict of interest arises when a doctor has a professionally-related commercial or financial interest.\textsuperscript{520} Such interests include consultancies, commercial support of educational meetings,

\textsuperscript{516} Id. at 483–84.
\textsuperscript{517} Id. at 484.
\textsuperscript{518} Id.
\textsuperscript{519} See supra notes 332–70 and accompanying text.
contracts with economic incentives, implied obligations to promote a product, and drug-company gifts. The advisory opinion requires these potential conflicts to be disclosed to the patient.

Some argue that disclosure is insufficient to solve the problems created by conflicts of interest. Economic scholars have found that people do not really understand conflicts of interest and that disclosure may enhance trust, rather than inject skepticism into the process. Since most people are inclined to trust their doctors, they are confident their doctor will overcome the conflict, especially when it is voluntarily disclosed. Reflecting this view is the recent article in the Journal of the American Medical Association proposing that because of their leadership role in the profession, academic medical centers should adopt policies to address many of the common pharmaceutical marketing practices that create conflicts of interest. Specifically, it urges medical centers to adopt policies to eliminate or modify practices including providing small gifts, meals, and samples, continuing medical education, speakers’ bureaus, ghost-writing, and consulting and research contracts.

Although I agree that prohibition is preferable, disclosure is a feasible step in the right direction. First, disclosure will educate the public about drug company practices and may inject a bit of caution. While the research is limited, one study found that “patients are more likely than doctors to believe that gifts may influence prescribing behavior and that patients tend to view gifts that influence prescribing behavior as inappropriate.” This suggests that a better-informed patient will be a more cautious patient, which would be a welcome counterweight to the excessive influence of industry marketing. Second, unlike the recent AMA proposal which is limited to medical schools, the informed consent requirement would apply to all doctors, whether in an

521. Id.
522. Id.
525. Id. at 5-6.
527. Id. Some academic medical centers are already taking steps to implement these proposals. For example, the U.C. Davis Medical Center is considering three recommendations which would (1) ban gifts, meals, travel expenses, payment for attending meetings or participating in online CME; (2) ban free samples (which would be replaced by a voucher system for low-income patients); and (3) exclude medical professionals with ties to drug or device manufacturers from committees that oversee drug or device purchasing. Dorsey Griffith, UCD May Curb Doctors’ Drug-Company Freebies, SACRAMENTO BEE, Oct. 3, 2006, at A1.
528. See supra note 37 and accompanying text regarding the current political clout of the drug industry; see also Okie, supra note 66, at 1063-64.
academic medical center or a community practice. Third, in contrast to the AMA proposal, which lacks any enforcement mechanism, the risk of tort liability gives informed consent teeth and should discourage doctors from engaging in the most egregious practices. Finally, adopting an informed consent requirement will provide injured patients a remedy where doctors have failed to make adequate disclosures.

In the long term, the initiatives to study the impact of industry marketing on health care should focus academic researchers, medical practitioners, and patients and their advocates on the negative aspects of current practices. Requiring disclosure of marketing influences could be a useful complement to these initiatives. Over time this attention should lead to a critical mass of public opinion supporting appropriate restrictions on drug-company practices in the interest of patient safety, the ethical practice of medicine, and public health.

III. PROPOSED DISCLOSURES FOR OFF-LABEL PRESCRIPTIONS AND CONFLICTS OF INTEREST

Dr. Marcia Angell, former editor of the New England Journal of Medicine, composed a thoughtful set of questions for patients to ask their doctors to elicit information about off-label uses and conflicts of interest. But, in my view, this approach puts the burden on the wrong person. Most patients are unaware of the widespread practice of off-label prescribing and the billions of dollars the drug industry spends to influence prescribing decisions. Only the rare and exceptionally assertive patient will have the knowledge and courage to question her doctor as Dr. Angell suggests. Rather than putting the burden on the patient to inquire, I think the doctor should be required to affirmatively disclose this information. The disclosures I propose are set out below: Part III.A presents the proposed disclosures about off-label prescriptions, and Part III.B covers the proposed disclosures about conflicts of interest.

531. Id. at 110–11 (explaining that medical malpractice actions provide needed compensation to injured patients and actually undercompensate them for their medical expenses and lost income.)
532. See supra Part I.B.
533. Angell, supra note 7, at 261–62. Dr. Angell suggested that patients should ask the following:
What is the evidence that this drug is better than an alternative drug or some other approach to treatment? Has the evidence been published in a peer-reviewed medical journal? Or are you relying on information from drug company representatives? . . . Is this drug better only because it is given at a higher dose? Would a cheaper drug be as effective if it were given at an equivalent dose? . . . Are the benefits worth the side effects, the expense, and the risk of interactions with other drugs I take? . . . Is this a free sample? If so, is there a generic drug or an equivalent drug I can use that is cheaper when the free samples run out? . . . Do you have any financial ties with the company that makes this drug? For example, do you consult for the company? Other than free samples, do you receive gifts from drug companies? Are you being paid to put me on this drug and enroll me in a drug company study? Do you make time for visits from drug company representatives?
A. PROPOSED DISCLOSURE OF OFF-LABEL PRESCRIPTIONS

- Is this drug FDA-approved for treatment of this condition?
- If not, is there an FDA-approved alternative?
- If so, what are the advantages of the off-label treatment over the FDA-approved alternative?
- Is there a generic alternative?
- If so, what are the advantages of the off-label treatment over the generic alternative?
- What research supports the off-label use? What is the source of information about the off-label use? Has research about the off-label use been published in a peer-reviewed medical journal? Or are you relying on information from a drug-company representative or a drug-company sponsored CME program?

B. PROPOSED DISCLOSURES OF CONFLICTS OF INTEREST

- Do you have any financial ties to the drug manufacturer including stock ownership, a consulting contract, or membership on a speakers’ bureau?
- Are you conducting Phase IV trials on this drug? Will you receive any compensation for prescribing this drug to the patient?
- Have you attended CME programs sponsored by the manufacturer? Did the manufacturer provide the program at no cost to you? Did it pay your expenses or provide you any compensation or gifts for attending?
- Did you receive this drug as a free sample from the drug company?
- Have you accepted any other gifts from the manufacturer?

CONCLUSION

Patients need to know the facts about off-label uses and conflicts of interest to make well-informed health care decisions. Off-label prescribing is in itself a concern, especially where research on the off-label use is inadequate and FDA-approved alternatives are available. Aggressive marketing is in itself a concern, especially where it creates conflicts of interest for doctors. Together they expand the market for treatments unsupported by any reliable scientific research, drive up the cost of health care, and jeopardize patient safety. While disclosure of this information may cause some patients to be reluctant to consent to proposed treatments, this reluctance is an appropriate counterbalance to the drug industry’s excessive influence on prescribing decisions.