Prosecutions of Pharmaceutical Companies for Off-Label Marketing: Fueled By Government’s Desire to Modify Corporate Conduct or Pursuit of a Lucrative Revenue Stream?

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INTRODUCTION

It has been estimated that health care fraud and abuse costs the federal government tens of billions of dollars every year.1 Admirably, government officials actively root out fraud and aggressively seek penalties to recoup some of the dollars lost on fraudulent expenditures. Hundreds of civil and criminal investigations are currently ongoing against the health care industry brought by the federal government, along with associated investigations by state attorneys general.2 Recently, Attorney General Eric Holder stated during the National Summit on Health Care Fraud that:

In 2009, the Justice Department reached an all-time high in the number of health care fraud defendants charged, more than 800. We also obtained more than 580 convictions. And on the civil enforcement front, our health care fraud recoveries last year under the false Claims Act exceeded a stunning $2.2 billion dollars.3

In this environment, it is becoming almost commonplace for large pharmaceutical companies to settle single fraud and abuse cases brought by

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1. Donald M. Berwick & Andrew D. Hackbarth, Eliminating Waste in US Health Care, 307 JAMA 1513, 1514 (2012). In this April 2012 study, former CMS Administrator Donald M. Berwick and RAND Corporation analyst Andrew D. Hackbarth estimated that fraud and abuse added as much as $98 billion to Medicare and Medicaid spending in 2011.
2. Id.
the government for hundreds of millions or even billions of dollars, rather than risk the stiff fines and possible “corporate death penalty” of exclusion from doing business with the government under Medicare, Medicaid, and other federally-funded health care programs. Many of these high-profile cases involve allegations that the companies callously and blatantly promoted their products for purposes that are not approved by the United States Food and Drug Administration ("FDA"), putting profits before safety in disregard for public health.4

Under the Federal Food, Drug and Cosmetic Act ("FDCA"), as interpreted by the government, pharmaceutical manufacturers may not “promote” their products for any “off-label” use that is not approved by the FDA.5 Drug companies have an obvious financial motivation to increase drug sales, whether for indicated or off-label uses. Some commentators take comfort in the fact that the spread of false information is deterred by the current regulatory system, which exposes the manufacturer to potential liability under both criminal and civil laws and sometimes results in personal liability on the part of corporate officers. The government has a number of tools to prosecute off-label promotion.6 And it has done so with a vengeance over the last decade, primarily invoking the False Claims Act.7 A journalist for the Chicago Tribune recently concluded after reviewing the dozens of massive settlements in cases involving off-label promotion of drugs and other health care fraud, even when companies are faced with large fines “[i]t is still good business to promote drugs illegally.”8 According to Eric Blumberg, a litigation deputy for the FDA’s office of chief counsel, “[t]he government needs to start prosecuting individuals if [it] want[s] to deter this conduct.”9

Current regulatory law in the United States, however, lacks clarity with

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4. See infra Section II.B, listing many of the high-profile investigations that were settled for high dollar figures.
5. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 331(a), (b), 352(a) (2011); see also statutes cited infra notes 12-16.
6. See U.S. GOV’T ACCOUNTABILITY OFFICE, GAO-08-835, Prescription Drugs: FDA’s Oversight Of The Promotion Of Drugs For Off-Label Uses 19, 26 (2008), available at http://www.gao.gov/assets/280/278832.pdf (discussing the FDA’s review of promotional materials and options for addressing materials that violate the prohibition on off-label marketing). Options available for prosecuting off-label promotion include the FDA’s issuing regulatory letters, issuing violations, and referring matters to the DOJ for enforcement action of the type discussed infra.
9. Id.
respect to the specific conduct that is or is not permissible when the pharmaceutical company communicates information about its products. It is reasonable to question whether the regulations as interpreted are appropriately and narrowly tailored, because they unquestionably make it illegal to disseminate even truthful, scientific information about the product if it relates to an off-label use. The criminalization of this information and the prospect of the additional suits that often trail behind a U.S. Department of Justice (“DOJ”) allegation creates a strong incentive to curtail not only more questionable marketing practices, but also to research and disseminate truthful information about the drug’s applicability to other conditions and populations that may not be profitable enough to warrant seeking a labeling change.

Section I of this article begins by tracing the federal regulations in the FDCA that govern pharmaceutical company information about off-label uses of drugs. This section includes discussion of the expansive definition of drug “labeling” and the statutory prohibition on selling “new” or “misbranded” drugs. Section II turns to the DOJ’s aggressive enforcement of perceived regulatory violations, such as those arising from off-label marketing, primarily under the False Claims Act. This enforcement typically includes the government’s draconian threat of exclusion, which bars a company from doing business with the federal government under health care programs such as Medicare and Medicaid. Section III explores two serious concerns that call into question the DOJ’s aggressive approach: (A) the prevalence of off-label prescription drug use in health care today, and the dichotomy between what the physician can prescribe and the drug company can discuss; and (B) the shaky constitutionality of the government’s attempts to regulate speech in this area. Next, in Section IV, several factual examples of government prosecutions are explored, including some of the fundamental challenges to them with a spotlight on the question of whether the restrictions on industry inure to the public interest. In Section V, this paper highlights the added financial costs that often follow DOJ scrutiny, in the form of suits by zealous state attorneys general and allegedly-aggrieved consumers, third party payors, and shareholders. Finally, Section VI addresses the important health policy at issue, and asks whether the current enforcement environment is changing industry conduct and leading to public benefit.

In the end, this article questions the premise that the massive settlements of recent years are “good” for the public, and that the payment of these astronomical sums is viewed by industry as merely a “cost of doing business.” There is a serious problem with these prosecutions due to the lack of certainty on the part of the pharmaceutical industry about what is, and what is not, permissible in “detailing” the product and providing
scientific and educational material to physicians. One can reasonably
question whether the government’s goal is to induce a change in industry
conduct, as opposed to continuing to generate a windfall and substantial
revenue stream for government, with no reasonable expectation that
conduct is actually being modified. The practice “may enrich the United
States Treasury at the expense of consumers from whom the costs will be
extracted.”

I. FDCA REGULATION OF INFORMATION ABOUT
OFF-LABEL USES OF DRUGS

Regulations regarding the approval process and subsequent sale of
pharmaceuticals are set forth in the Federal Food, Drug, and Cosmetic Act
of 1938, as amended (“FDCA”). The United States Food & Drug
Administration (“FDA”) is the agency authorized to regulate the promotion
of prescription drugs. The FDCA does not discuss whether a drug
manufacturer may distribute or communicate any information about
potential off-label uses of its approved drugs.

However, the FDCA provision regarding new drugs, coupled with
regulations promulgated by the FDA, essentially acts to regulate off-label
promotion. The FDCA expressly prohibits the introduction of a “new
drug” into commerce. A new drug is defined as one which is “not
generally recognized . . . as safe and effective for use under the conditions
prescribed, recommended, or suggested in the labeling.” Further,
regulations make it clear that a drug that has been approved for use to treat
some condition in some population, may nonetheless be a new drug
depending on its label: “the newness of a drug may arise by reason (among
other reasons) of . . . [t]he newness of use of such drug in diagnosing,
curing, mitigating, treating, or preventing a disease, or to affect a structure
or function of the body, even though such drug is not a new drug when used
in another disease or to affect another structure or function of the body.”
If a manufacturer distributes a drug with a label other than that approved by
the FDA, it is considered a new drug.

10. Vicki Girard, Punishing Pharmaceutical Companies for Unlawful Promotion of
Approved Drugs: Why the False Claims Act Is the Wrong Rx, 12 J. HEALTH CARE L. & POL’Y
119, 130 (2009).
Labeling includes all “written, printed, or graphic” materials that accompany the drug. The FDA’s authority in the area of off-label marketing arises from its expansive definition of “label.” The FDA regulations have been interpreted to sweep more broadly than the plain language of the statute in prohibiting communications by the manufacturer in many contexts. The regulations have been used to control advertising and even discussions between the drug manufacturer and physicians. Indeed, “in combination with its authority over promotional labeling, the FDA’s regulatory oversight of prescription drug marketing extends to practically every type of material and media imaginable.” One commentator noted that “FDA regulations restrict company activities in this area to a much greater extent than the FDCA’s statutory scheme. For example, the FDA defines ‘labeling’ to include virtually anything that a company or its employees might produce or present.” Thus, the manufacturer may not make statements or provide information about its drug—even if true—without the approval of the FDA.

In addition to the prohibition on selling “new drugs,” the FDCA prohibits the sale of a “misbranded” drug. A drug is considered misbranded if it includes inadequate directions for use, or if the labeling bears false and misleading information. In practice, if the manufacturer provides information to a prescriber relating to an off-label use, the government will argue that the approved label is inadequate and/or misleading because that labeling does not address the safety and efficacy of the drug for that off-label use. As with defining what a new drug is, the misbranding provisions have been interpreted as constituting any false or misleading statements in the labeling or materials provided with the drug, including directions for use. The “intended use” of the product has been interpreted to include any use that the manufacturer intends based on the label, advertisements or any statements made to physicians. Thus, arguably if

24. 21 U.S.C. §§ 352 (f) and (a) (defining “inadequate directions for use” and “false and misleading label,” respectively).
25. 21 U.S.C. §§ 352 (f) and (a).
27. 21 C.F.R. § 201.128 (2012).
any statement is made regarding a use that is not included in the FDA-approved labeling, then the drug has been “misbranded.” 28

Another commentator argues that: “[m]any regard this interpretation as awkward at best and untenable at worst.” 29 On the other hand, courts have held that it is a question of fact whether labeling is false or misleading. 30 Therefore, expert testimony regarding safety and efficacy could show that information communicated regarding an off-label use was not, in fact misleading. 31

If a company introduces a drug into interstate commerce, a misdemeanor violation occurs if the drug qualifies as either a new drug or misbranded under the FDCA. 32 For a misdemeanor, the regulations do not require any specific intent to mislead. 33 To prove a felony, the government must show intent to defraud or mislead. 34

The government’s broad interpretation of the regulatory framework would seem justified in contexts where there is strong evidence that the pharmaceutical company made blatantly false statements to physicians to encourage increased use of a drug for an unapproved purpose. However, as will be discussed infra, the evidence is not always so clear; yet, companies are not in a position to battle the government to a conclusion on the merits when exclusion from participation in government-funded healthcare programs is threatened. For example, in United States ex rel. Franklin v. Parke-Davis, drug company Parke-Davis argued that the FCA relator failed to show that Parke-Davis made any material false statement. 35 The court held that to pursue the prosecution, the government need not show that Parke-Davis lied to physicians about safety or efficacy to induce prescriptions. 36 Rather, it was enough that the company promoted an unapproved use. 37

In sum, when a drug company promotes in a way that is inconsistent with

29. Id. at 310; see also Allison D. Burroughs, et al., Off-Label Promotion: Government Theories of Prosecution and Facts that Drive Them, 65 FOOD & DRUG L.J. 555, 563 (setting forth an untested but clear argument regarding why drugs should be exempt from the “adequate directions for use” provision of the misbranding statute).
30. E.g., United States v. An Article of Drug Consisting of 47 Bottles, More or Less, Jenesol RJ Formula ‘60’, 320 F.2d 564, 571 (3d Cir. 1963); Colusa Remedy Co. v. United States, 176 F.2d 554, 561 (8th Cir. 1949).
34. Id.
36. Id.
37. Id.
the label, the FDCA gives rise to charge that the company either:

1) introduced a new drug into commerce under 21 U.S.C. § 331(d) (prohibiting the introduction or delivery for introduction into interstate commerce of a “new drug” as defined under §355 of the FDCA); or

2) misbranded the drug under 21 U.S.C. § 331(a) (prohibiting the introduction or delivery for introduction into interstate commerce of any drug that is misbranded); § 352(a) (defining any drug as misbranded if its labeling is false or misleading); or § 352(f)(1) (defining as misbranded if it lacks adequate directions for use).38

II. THE DECLINE OF FDA ACTION AND EMERGENCE OF AGGRESSIVE DOJ ENFORCEMENT

Until recently, the FDA exercised nearly exclusive regulatory authority over pharmaceutical companies’ promotional activities related to prescription drugs.39 The FDA has rarely pursued punitive sanctions.40 Perhaps this restraint is driven, at least in part, by the need for partnership between the Agency and the pharmaceutical industry in pursuit of good science and the interests of public health. Certainly, there is a long history of the FDA reviewing drug company advertising, and on occasion sending warning letters and the like, and instructions to cure misleading messages. Given the staggering number of advertisements and communications between drug companies and the medical community, however, this has proven not to be a robust method of enforcement. Further, as will be discussed in Section V, infra, the constitutionality of the FDA’s regulation of off-label uses has been successfully challenged in the courts, and some have speculated that this has led to reduced enforcement. Whatever the reason for FDA restraint in enforcement, the DOJ has emerged in the last decade as a more “strident crusader” in searching for violations of the off-


In recent years, the DOJ dramatically expanded its prosecutions for off-label marketing using the False Claims Act (“FCA”). Although claims for violations of the FDCA may be included in these prosecutions, the FCA has become the “primary vehicle for government health care fraud enforcement,” which carries the potential for both criminal and civil liability.

Under the FCA, a company is liable to the government if it “knowingly presents, or causes to be presented... [to the government] a false or fraudulent claim for payment or approval.” Qui tam suits are common under the FCA. These involve a private citizen (referred to as the relator or sometimes as a “whistleblower”) bringing suit against the drug company on behalf of the government. The matters are filed under seal and the government is given an opportunity to investigate the allegations and determine whether to intervene in the suit. If there is a recovery, the private individual can collect between fifteen to thirty percent of the government’s recovery plus attorneys’ fees and costs. Thus, private individuals have a powerful incentive to blow the whistle.

A typical FCA suit against a drug company will allege that the company systematically promoted the drug for an off-label use, and that this promotion caused physicians to prescribe the medicine for that use, in turn leading to payments by the government—usually under Medicare or Medicaid—for such off-label prescription. These suits are usually civil in nature, although there is a criminal FCA counterpart. It has been postulated that the government believes the “false claims” theory is too attenuated for use in a criminal prosecution, and thus uses the FDCA criminal provisions, which were described in Section I above.

Because the FCA is a fraud statute, claims under it must be pled with particularity, consistent with Federal Rule of Civil Procedure 9(b). Some FCA cases have been dismissed when the relator did not plead with

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41. Girard, supra note 10, at 126.
47. Burroughs, supra note 29, at 557.
48. FED. R. CIV. P. 9(b).
particularity the details of any false claim for government reimbursement.\textsuperscript{49} Because the drug companies themselves do not submit claims for reimbursement to the government, the FCA theory is that the company’s unlawful marketing for an off-label use is the reason a physician prescribed the medication.\textsuperscript{50}

According to some courts, even a truthful statement made by the drug company can be the foundation of a false claim based on “misbranding” if the use is off-label.\textsuperscript{51} The court in Parke-Davis found that a violation of the FDCA for off-label promotion may be sufficient in itself to establish liability under the FCA, whether or not the underlying promotional statements were false.\textsuperscript{52} Thus, the FCA does not require both a false statement and a false claim under the court’s ruling. Parke-Davis had argued that forty-two state Medicaid programs permitted off-label prescriptions and, thus, there were no “false claims” made in those states.\textsuperscript{53} The court disagreed, noting that the relator had treatment histories of many patients that reflected the drug was prescribed off-label, which was illegal in at least some states.\textsuperscript{54} Parke-Davis also argued that because it did not directly submit claims to the government, it therefore did not “cause” a false claim to be submitted.\textsuperscript{55} The court disagreed on this point too, holding that company acts could be a “substantial factor” in the physicians’ prescriptions leading to the claims for reimbursement that were ultimately made.\textsuperscript{56}

Importantly, the Fraud Enforcement and Recovery Act (“FERA”) was enacted in 2009, revising aspects of the FCA.\textsuperscript{57} Under the statute, there can be liability even when the false claim was not submitted to the government, but to a private contractor or agent, thus removing one protection that certain cases had applied previously.\textsuperscript{58} The definition of “claim” was broadened and the statute of limitations expanded.\textsuperscript{59}

\textsuperscript{49} U.S. \textit{ex rel.} Roop v. Hypoguard USA, Inc., 559 F.3d 818, 825-26 (8th Cir. 2009); \textit{see also} Burroughs, \textit{supra} note 29, at 558.

\textsuperscript{50} \textit{See U.S ex rel.} Kennedy v. Aventis Pharm., Inc., 512 F. Supp. 2d 1158, 1163 (N.D. Ill. 2007).


\textsuperscript{52} \textit{Id.}

\textsuperscript{53} \textit{Id.} at *3.

\textsuperscript{54} \textit{Id.}


\textsuperscript{56} \textit{Franklin}, 2003 WL 22048255 at *6; \textit{Franklin}, 147 F. Supp. 2d at 52-53.


\textsuperscript{58} \textit{See Id.} at 1621-25.

\textsuperscript{59} \textit{See Id.} at 1622-23.
B. Penalties and Exclusion

The FCA provides for civil penalties of $5,000.00 to $10,000.00 for each false claim submitted.60 Thus, if the government can show substantial off-label prescription, the fine mounts swiftly. Also, the damages in an FCA matter can be triple the amount actually billed to the government.61 In recent settlements, pharmaceutical companies have paid billions to resolve some prosecutions. A November 13, 2011 Chicago Tribune article62 reported on known settlements with the DOJ, and the settlement amounts were staggering:

<table>
<thead>
<tr>
<th>Company</th>
<th>Drug(s)</th>
<th>Year</th>
<th>Settlement amount</th>
<th>Infraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>GlaxoSmithKline</td>
<td>Avanda, etc.</td>
<td>2011</td>
<td>$8.0 million</td>
<td>Though the case is ongoing, Glaxo has said it will pay $3 billion to settle allegations that include illegally marketing diabetes drug Avanda and others.</td>
</tr>
<tr>
<td>Pfizer</td>
<td>RXBRA, etc.</td>
<td>2019</td>
<td>$2.3 billion</td>
<td>Approved to treat arthritis pain, Bextra was marketed more broadly as an all-purpose painkiller in recommended doses larger than those for which it was approved.</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Zyprexa</td>
<td>2019</td>
<td>$1.4 billion</td>
<td>The anti-psychotic was approved to treat schizophrenia and bipolar disorder but also was marketed as a treatment for dementia.</td>
</tr>
<tr>
<td>Sereno</td>
<td>Serostim</td>
<td>2015</td>
<td>$704 million</td>
<td>The drug was approved for AIDS wasting, or often-fatal condition involving severe weight loss. Sereno pleaded guilty to promoting unapproved diagnostic tools to boost sales.</td>
</tr>
<tr>
<td>Purdue</td>
<td>OxyContin</td>
<td>2007</td>
<td>$635 million</td>
<td>When doctors became convinced that the painkiller was highly addictive, the company circulated to its sales force false claims that it was less addictive than other drugs.</td>
</tr>
<tr>
<td>Allergan</td>
<td>Botox</td>
<td>2010</td>
<td>$600 million</td>
<td>Botox is approved for several uses, including eye-muscle disorders and excessive underarm sweating. The company advertised it for ailments such as muscle spasticity.</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Serquel</td>
<td>2010</td>
<td>$120 million</td>
<td>Psychiatric drug Serquel was marketed for unapproved uses, such as treating insomnia and Alzheimer’s disease.</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>Abilify</td>
<td>2007</td>
<td>$115 million</td>
<td>Abilify, approved to treat adult schizophrenia and bipolar disorder, was marketed for pediatric use and dementia-related psychosis. Also included was a kickback scheme.</td>
</tr>
<tr>
<td>Schering-Plough</td>
<td>Temodar, stron-A</td>
<td>2004</td>
<td>$435 million</td>
<td>Temodar used for a specific type of brain tumor, was marketed for other brain cancers. Intron A was marketed for use in treatment of bladder cancer and hepatitis C.</td>
</tr>
<tr>
<td>Pfizer, Warner- Lambert</td>
<td>Neurontin</td>
<td>2004</td>
<td>$430 million</td>
<td>Neurontin was approved for anti-seizure use by epilepsy patients. It was marketed to relieve pain and treat headaches and psychiatric illnesses such as manic depression.</td>
</tr>
</tbody>
</table>


Note: according to several sources, 64 Fed. Reg. 47099, 47104 at § 85.3(a)(9) established a mandatory range for FCA penalties between $5,500 and $11,000.


Pharmaceutical companies have conceded to more high-dollar settlements with the DOJ in the short time since that article was published. These settlements increasingly also address the state actions that now commonly follow in the wake of aggressive DOJ action against a pharmaceutical company. In May 2012, Abbott announced a $1.6 billion settlement to resolve allegations related to alleged off-label marketing of anti-seizure drug Depakote. The settlement included a criminal fine and forfeiture of $700 million. It also included a civil settlement to resolve false claims allegations, which involved a $560 million payment to the federal government and payment of $240 million to resolve the claims of forty-nine states and the District of Columbia. Additionally, Abbott agreed to pay a further $100 million to states to resolve consumer protection claims.

In the summer of 2012, Johnson & Johnson agreed in principal to resolve several off-label marketing allegations related to anti-psychotic Risperdal. The settlement with the federal government to

63.  Id. at 2.
64.  For more information of tag-along state actions, see discussion infra Part V.A.
66.  Id.
67.  Id.
69.  Jonathan D. Rockoff & Joann S. Lublin, J&J Penalty May Total $2.2 Billion:
resolve both criminal and civil claims is expected to total as much as $2.2 billion.\textsuperscript{70} Johnson & Johnson also agreed to settle thirty-six states’ and the District of Columbia’s claims for $181 million, combined.\textsuperscript{71}

Despite the substantial fines that can be exacted on a company for FCA violations, these enormous settlements may be driven by corporate fear of exclusion, rather than of monetary damages. Exclusion is an administrative sanction that is imposed by the Department of Health and Human Services (“HHS”), barring individuals and entities from participating in federal health care programs, including Medicare and Medicaid, if they have been convicted of certain crimes or had other enforcement taken against them.\textsuperscript{72} Exclusion is mandatory if the individual or entity has been convicted of a felony related to health care fraud.\textsuperscript{73} Additionally, HHS has discretion to exclude individuals or entities that have been found guilty of misdemeanor fraud, either health care-related or non-health care-related,\textsuperscript{74} including fraud under the FDCA.\textsuperscript{75} These FCA exclusion rules were significantly expanded in 1998.\textsuperscript{76} HHS revised the rule to give the Office of Inspector General (“OIG”) the authority to exclude drug manufacturers from receiving federal health care program reimbursements if they are found to have engaged in significant financial or other impropriety.\textsuperscript{77}

Corporate officers as well as companies can be excluded, even when there is no evidence that they had personal knowledge of the conduct that


70. \textit{Id.}
73. § 1320a-7(a)(3).
74. §§ 1320a-7(b)(1)(A)(i)-(ii), 1320a-7(b)(1)(B).
75. See discussion supra Part I.
led to the misdemeanor conviction. In Friedman v. Sebelius, the court described the responsible corporate officer doctrine and explained that:

‘[T]he liability of the managerial officers did not depend on their knowledge of or personal participation in, the act made criminal by the statute,’ but rather on ‘an omission or failure to act’ when the agent, ‘by virtue of the relationship he bore to the corporation, . . . had the power to prevent the act complained of.’

The threat of exclusion has been described as the corporate “death sentence.” Pharmaceutical companies faced with exclusion in off-label marketing matters have demonstrated a decided aversion to testing whether an exclusion will be imposed. Even if an exclusion were to be ultimately overturned on appeal, by that time, it might well be too late for the company’s survival.

It is up to the various government prosecutors to decide whether to seek permissive exclusion, and the decision rests with the Secretary of Health and Human Services. When faced with a government prosecution, pharmaceutical companies have particularly limited bargaining power when there is a threat of corporate exclusion and potential for vicarious liability and personal exclusion of executives. Settlement looks more attractive when juxtaposed with the costs of defense and perhaps the prospect of public disclosure of inflammatory documents regarding marketing practices, even when those may be merely by a rogue drug representative who overzealously tried to increase sales by pushing off-label prescriptions.

Finally, as OIG itself recognized, it often:

[N]egotiates compliance obligations with health care providers . . . as part of the settlement of . . . investigations arising under a variety of civil . . . false claims statutes . . . A provider . . . consents to [these obligations] . . . in exchange for OIG’s agreement not to seek to exclude that . . . entity from participation

78. See e.g., 42 U.S.C. § 1320a-7(a)(1)(A)(ii) (“The secretary may exclude . . . from participation in any Federal health care program . . . [a]ny individual . . . that has been convicted . . . of a . . . misdemeanor relating to fraud, theft, embezzlement, breach of fiduciary responsibility or other financial misconduct with respect to any act or omission in a health care program”).


81. 42 U.S.C. § 1320a-7(b).
in Medicare, Medicaid and other Federal health care programs.\textsuperscript{82}

III. THE GOVERNMENT AGGRESSIVELY PURSUES OFF-LABEL MARKETING DESPITE TWO SERIOUS CONCERNS

A. The Off-Label Prescription of Drugs is Legal and Sometimes Medically Necessary

Off-label uses include the prescription of the drug at a dose not approved in the label, to a patient population not approved, or to treat a condition either not considered or considered and rejected by FDA. What is essential to understand, and difficult to accept analytically, is that physicians can legally prescribe FDA-approved drugs for any therapeutic use that is appropriate in their medical judgment.\textsuperscript{83} Given the expansive regulatory interpretations,\textsuperscript{84} it might seem surprising that the courts and government expressly recognize that off-label use 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{85} Off-label use is widespread in the medical community and often is essential to giving patients optimal medical care.\textsuperscript{86} As the statute itself reflects, “nothing in the Food and Drug and Cosmetic Act shall be construed to limit or interfere with the authority of a healthcare practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease.”\textsuperscript{87} “A physician may prescribe a legal drug to serve any purpose that he or she deems appropriate, regardless of whether the drug has been approved for that use by the FDA.”\textsuperscript{88} This arrangement leads to a “certain ‘asymmetry’ in the regulation of off-label uses: while physicians may lawfully prescribe drugs for off-label uses, the FDCA generally prohibits manufacturers from marketing these uses to physicians.”\textsuperscript{89}

Off-label drug prescriptions are very common in medical practice. By one account, over twenty percent of all prescriptions are off-label.\textsuperscript{90} In some fields, off-label use is even more prevalent. For example, The

\begin{footnotesize}
\textsuperscript{82} Notice for Potential Monitors for Quality-of-Care Corporate Integrity Agreements, 74 Fed. Reg. 52,964, 52,964-65 (Oct. 15, 2009).
\textsuperscript{83} Use of Approved Drugs for Unlabeled Indications, 12 FDA Drug Bull. 1 at 4-5 (1982).
\textsuperscript{84} See discussion supra Part I.
\textsuperscript{86} Id.
\textsuperscript{87} 21 U.S.C. § 396.
\textsuperscript{89} In re Schering Plough Corp. Intron/Temodar Consumer Class Action, 678 F.3d 235, 240 (3d Cir. 2012).
\end{footnotesize}
American Society of Clinical Oncology reported that an astounding fifty percent to seventy percent of cancer treatments are prescribed off-label. In pediatrics, it is well known that although many drugs have not been tested in children and therefore cannot include label directions for use in children, they nonetheless may be the only effective treatment in the pediatric population. A similar situation exists in elderly populations. Medicare and private insurers pay for some off-label uses of drugs, and such can be considered state of the art. Without off-label prescribing, key populations of patients may go without needed medicine.

Just as clearly, however, off-label prescription of drugs can be dangerous and sometimes is based on unproven assumptions about benefit and risk. For those uninitiated in the complex and expensive New Drug Application process, it may seem desirable for pharmaceutical companies to test drugs in all patient populations, at all doses and for all disease endpoints. It is beyond the scope of this paper to discuss in detail the new drug approval process. But the nature of the rigorous testing the FDA justly requires to prove both safety and efficacy leads to narrowly-focused testing protocols where the drug is given to a discrete population of patients, at specific doses, and for specific diseases or conditions. Once years of testing have been completed and the drug is approved for sale, it often is not in the manufacturer’s best interest—nor is it required by any regulation—to begin again to test the drug in other populations. As aptly described by one commentator,

[T]hough new indications may be added to a drug’s label through a supplemental new drug application, this occurs infrequently: generic drugs lack a corporate sponsor to bear the required expenses, and for brand-name drugs that are already widely used off-label, conducting a costly clinical trial that could produce non-supportive evidence is a potentially risky business decision.

Thus, whether a drug is effective either for conditions/diseases other than those approved in the label or in populations other than those in which it was tested, is often a question left to the medical community to determine after the drug is on the market.

91. Id. at 235; see also Girard, supra note 10, at 131.
92. Kesselheim, supra note 90, at 225.
93. Burroughs, supra note 29, at 556.
94. Kesselheim, supra note 90, at 235-38; see also Randall S. Stafford, Regulating Off-Label Drug Use—Rethinking the Role of the FDA, 358 N. ENGL. J. MED. 1400, 1427 (2008).
95. See generally Applications For FDA Approval To Market A New Drug, 21 C.F.R. § 314.
96. Stafford, supra note 94, at 1427.
PROSECUTIONS OF PHARMACEUTICAL COMPANIES

B. It is Constitutionally Questionable for Government to Limit Truthful Commercial Speech About Off-Label Uses

The regulations and enforcement actions discussed herein give rise to serious questions about whether, and when, the government can prevent the truthful exchange of scientific information between a drug company and a physician or other health care providers. In July 2008, the United States Government Accountability Office (“GAO”) submitted a Report to the U.S. Senate entitled “Prescription Drugs: FDA’s Oversight of the Promotion of Drugs for Off-Label Uses.” Although focused on the facts of FDA regulatory positions, and not the constitutionality of those positions, the GAO reflects the incongruity of the restrictions on speech:

FDA does not generally regulate the exchange of scientific information, but when such information is provided by or on behalf of a drug company regarding one of the company’s products, the information may be subject to the labeling and advertising provisions of the law and regulations. For example, while information provided at CME programs – such as medical conferences and professional gatherings intended to enhance physicians’ knowledge and enable them to meet certain practice requirements – is not generally subject to FDA regulation, it will be if the program has been funded and substantially influenced by a drug company. Similarly, FDA’s position is that companies may respond to unsolicited requests for information from health care professionals, even if responding to requests requires the companies to provide information regarding off-label uses.

It is reasonable to question whether these rather fine distinctions regarding when and by whom truthful information may be shared with physicians inure to the best interests of the medical community and the public. If off-label uses are recognized as appropriate and necessary in certain circumstances, why limit when and how industry can speak?

Burroughs et al. succinctly traced the First Amendment concerns in this context. The constitutional question sprang from the December 1997 FDA Guidance on Industry-Supported Scientific and Educational Activities (“Guidance”). Not surprisingly, the Guidance described a drug company’s dissemination of scientific information as “promotional

98. Id. at 9.
material” which can be regulated; but it noted that the same information is not promotional and subject to regulation when circulated by the CME provider, or even by the drug company in response to a specific question. 101

Soon thereafter, the Washington Legal Foundation brought a lawsuit raising a First Amendment challenge to the regulation. 102 The court ruled in favor of the Foundation noting that under the FDA approach “a great deal of truthful information will also be embargoed. In this case, the truthful information may be life saving information, or information that makes a life within a debilitating condition more comfortable.” 103 Next, the Food and Drug Modernization Act was passed, amending the FDCA and subjecting a manufacturer to criminal penalties for the dissemination of information. 104

In 1999, the district court ruled in Washington Legal Foundation v. Friedman that this statute barred truthful speech about off-label uses and violated the First Amendment. 105 On appeal, the FDA abandoned its position and stipulated that neither the Guidance document nor the new legislation “provides the FDA with independent authority to regulate manufacturer speech.” 106

The United States Supreme Court subsequently found a different provision of the legislation to be unconstitutional. 107 The basis for the decision is instructive of how the Court would likely view the restrictions discussed herein. In Thompson v. Western States Medical Center, the FDA sought to regulate the “compounding” of “new” drugs by pharmacies. 108 In particular, the FDA sought to ban any advertising that compounded drugs are available. 109 The government argued that the “FDA’s experience with drug regulation demonstrates that proof of the safety and effectiveness of a new drug needs to be established by rigorous, scientifically valid clinical studies because impressions of individual doctors, who cannot themselves compile sufficient safety data, cannot be relied upon.” 110

The challenge to the legislation noted that obtaining approval from the FDA is costly and would effectively eliminate the availability of compounded drugs for those patients who have no alternative treatment. 111

103. Id. at 73.
108. Id.
110. Id. at 368-69.
111. Thompson, 535 U.S. at 369.
According to the Court, the government had argued that speech restrictions are justified because there is fear that advertising compounded drugs would lead to people getting them even if they do not need them.\(^{112}\) Tellingly, the Court rejected this logic:

Aside from the fact that this concern rests on the questionable assumption that doctors would prescribe unnecessary medications... this concern amounts to a fear that people would make bad decisions if given truthful information about compounded drugs..... We have previously rejected the notion that the Government has an interest in preventing the dissemination of truthful commercial information in order to prevent members of the public from making bad decisions with the information.\(^{113}\)

In the end, the Supreme Court held that the FDA ban on advertising of compounded drugs was unconstitutional because it did not satisfy the \textit{Central Hudson}\(^{114}\) test setting forth the protections governing commercial speech. After these challenges, and presumably because of them, the FDA often has not aggressively enforced the off-label promotion rules. Thus, the DOJ false claims prosecutions have taken precedence.

Another case, \textit{Sorrell v. IMS Health, Inc.},\(^{115}\) considered a Vermont statute that attempted to restrict pharmaceutical companies from using prescription data for marketing purposes when doctors and other parties are permitted to use the same data.\(^{116}\) The Supreme Court found that this restriction was content- and speaker-based, and rejected the state’s argument that it constituted mere commercial regulation.\(^{117}\) “[S]peech in aid of pharmaceutical marketing, however, is a form of expression protected by the Free Speech Clause of the First Amendment. As a consequence, Vermont’s statute must be subjected to heightened judicial scrutiny.”\(^{118}\) Vermont argued that its statute was intended to diminish the likelihood that marketing efforts would lead to prescription decisions that were in neither the patients’ nor the state’s best interests.\(^{119}\) Though significant, the Court found that these interests did not satisfy the heightened scrutiny standard and could not justify the restrictions imposed.\(^{120}\)

\(^{112}\) Id. at 370.
\(^{113}\) Id. at 374.
\(^{115}\) \textit{Sorrell v. IMS Health Inc.}, 131 S. Ct. 2653 (2011).
\(^{116}\) Id. \textit{See also VT. STAT. ANN. tit.18, § 4631(d) (2012).}
\(^{117}\) \textit{Sorrell}, 131 S. Ct. at 2663-67.
\(^{118}\) Id. at 2659.
\(^{119}\) Id. at 2658.
\(^{120}\) Id. at 2670-72.
Collectively, these opinions give rise to serious questions about whether the government’s current interpretation of the law could withstand constitutional scrutiny. Recently, the Second Circuit has held that it does not.\(^{121}\) In *Caronia*,\(^{122}\) the court found that a drug company representative’s truthful statements about off-label uses for the pharmaceutical Xyrem were protected under the First Amendment.\(^{123}\) Mr. Caronia was caught on tape promoting Xyrem for off-label uses, including the treatment of excessive pain associated with fibromyalgia.\(^ {124}\) Because Xyrem was approved by the FDA to treat only certain narcolepsy patients, the government charged Mr. Caronia with two misdemeanor counts of introducing a misbranded drug into commerce and conspiracy to introduce a misbranded drug into commerce in violation of 21 U.S.C. §§ 331(a) and 333(a)(2).\(^ {125}\) Echoing its argument in *Washington Legal Foundation*,\(^ {126}\) the government denied that it was attempting to regulate speech.\(^ {127}\) Rather, it claimed to introduce Mr. Caronia’s off-label promotional speech simply as evidence of his intent to conspire to sell a misbranded drug.\(^ {128}\) After a jury trial, Mr. Caronia was found guilty and sentenced to one year of probation, 100 hours of community service and a twenty-five dollar special assessment.\(^ {129}\)

On appeal of Mr. Caronia’s conviction, the majority relied heavily upon *Sorrell* and found that the FDCA’s misbranding provision must be subject to heightened scrutiny because it is a content- and speaker-based restriction and involves a criminal penalty.\(^ {130}\) Applying the four-pronged *Central Hudson* analysis, the Second Circuit held that the FDA misbranding regulations are too broad to support the government’s objective of promoting drug safety and public health and that government interests can be served equally well through more limited and targeted restrictions on speech.\(^ {131}\) Accordingly, even if speech can serve as evidence of a drug’s intended use, the court interpreted the misbranding provisions of the FDCA to not prohibit or criminalize “the truthful off-label promotion of FDA-approved prescription drugs.”\(^ {132}\) Therefore, “the government cannot

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121. United States v. Caronia, 703 F.3d 149, 168 (2d Cir. 2012).
122. Id.
123. Id.
124. Id. at 156.
125. Id. at 155, 157.
127. Caronia, 703 F.3d at 160-61.
128. Id. at 160.
129. Id.
130. Id. at 165.
131. Id. at 165-68.
132. Id. at 168.
Prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label use of an FDA-approved drug.”

Whether this rejection of the government’s ability to prosecute pharmaceutical manufacturers and their representatives for truthful speech about off-label uses will be followed in other Circuits remains to be seen.

IV. ILLUSTRATIVE FACTUAL SCENARIOS INVOLVING OFF-LABEL PROMOTION EVIDENCE

Undoubtedly, pharmaceutical company representatives sometimes “oversell” products for off-label uses, pushing profit before safety. As Kesselheim describes:

Detailing can lead to overuse of drugs with dangerous side effect profiles. [Vioxx] is a good example for this analysis. The drug was an analgesic, and thus the manufacturer could legally engage in promotion of its use to control certain types of pain.... However, the manufacturer’s multi-billion dollar promotional effort led to its widespread adoption outside of this narrow context. This became a public health disaster when rofecoxib was later publicly linked to cardiovascular complications.

If everything in the government’s many complaints against manufacturers is true, it would seem that there is an epidemic of this type of activity. But as discussed earlier, in light of the lack of clarity in the regulations regarding what is and is not lawful promotion, along with the fatal sanction of exclusion from participation in federal health care programs, the cases actually decided on the merits are few and far between. When cases settle, we are left without conclusive information about the true facts of the company’s conduct. Furthermore, as is so often seen in the context of mass tort litigation, judges and juries across the country reach conflicting decisions about the scientific merits of product liability cases every day. In the context of silicone breast implant litigation in the 1990s, for example, tens of thousands of cases were pending, and many were tried in front of a jury with conflicting results. In New Orleans, Louisiana and Reno, Nevada, spectacular jury verdicts against the silicone manufacturers were achieved by women with implants. Yet, in cases

133. Id. at 169.
134. Kesselheim, supra note 90, at 249.
involving the same product in Denver, Colorado\textsuperscript{137} and Portland, Oregon,\textsuperscript{138} the defense won. Indeed, when Federal Judge Sam Pointer held Rule 706 hearings before an independent panel of experts, it was concluded that implants did not, in fact, cause any disease.\textsuperscript{139} As time played out and more epidemiology studies were conducted, the legal community finally caught up with the scientific community, and it became widely accepted that implants did not lead to disease in women.\textsuperscript{140} This ultimate resolution would have been unimaginable to most, who had heard only about thousands of legal complaints and inflammatory news headlines.\textsuperscript{141}

Despite the difficulty in gaining a true understanding of the facts in off-label promotion matters brought by the DOJ, several cases have been described in literature or case law that illuminate the questions about the nature of the impact on public health from these cases.

The first criminal prosecution brought by the DOJ was against Genentech Inc. for the company’s violation of the FDA rules against promoting a drug for unapproved uses.\textsuperscript{142} The company’s product, Protropin, was a human growth hormone approved for use to treat undersized children who suffered from lack of adequate growth hormone.\textsuperscript{143} It was alleged that the company was marketing Protropin for “treatment of children who were undersized [due to] a rare form of juvenile obesity and [for] the treatment of burn patients.”\textsuperscript{144} The DOJ suggested that it could see patterns in the marketing practices of Genentech that led it to suspect that the company was marketing for off-label purposes.\textsuperscript{145} The company settled for fifty million dollars.\textsuperscript{146} Several years later, the same company was faced


\textsuperscript{140} See, e.g., COMMITTEE ON THE SAFETY OF SILICONE BREAST IMPLANTS, INSTITUTE OF MEDICINE, SAFETY OF SILICONE BREAST IMPLANTS 225-226 (Stuart Bondurant et al. eds. 1999) (discussing very substantial body of evidence that found no elevated risk of connective tissue disease in women with implants and concluding that there is no association between implants and connective tissue disease).


\textsuperscript{142} Girard, supra note 10, at 126.

\textsuperscript{143} See id.

\textsuperscript{144} Id.

\textsuperscript{145} Id.

\textsuperscript{146} Id.
with the rising off-label use of another of its products, Avastin.\textsuperscript{147} The product was approved in 2004 to treat colon cancer,\textsuperscript{148} and it was approved in 2006 to treat lung cancer.\textsuperscript{149} Then, in 2007, the company obtained approval to market a new drug called Lucentis that was based on the same active ingredient as Avastin, for macular degeneration, which is a leading cause of blindness in people over age sixty.\textsuperscript{150} Physicians developed methods of treating macular degeneration with the less expensive, older drug Avastin, although it was not approved for that use.

Genentech was placed in a very difficult position and was criticized for failing to facilitate the use of the much cheaper, older Avastin for macular degeneration. The company publically stated that while the medical community was acting “with noble intent, which is to help patients who are going blind as we speak . . . [,] there have been no safety and toxicity studies conducted on Avastin as an ophthalmic drug.”\textsuperscript{151} When asked how it communicated with the medical community about the issue, Genentech, previously stung by off-label promotion allegations in a different context, answered “[w]e make education material available to the doctors but we don’t take a position.”\textsuperscript{152} There was significant evidence about many aspects of the propriety of prescribing the product for this off-label purpose, but this purpose could not be freely discussed with physicians. After reviewing much of this information, one commentator concluded:

From a public policy perspective, it would be preferable to permit companies to act in an ethically responsible manner and to share fully any concerns about prevailing physician practice, rather than to limit communications to a brief press statement and the dissemination of peer-reviewed journal articles. But the current regulatory environment does not allow companies to do this.\textsuperscript{153}


\textsuperscript{150} See Osborn, supra note 22, at 336.


\textsuperscript{152} Id.

\textsuperscript{153} Osborn, supra note 22, at 338.
Company defenses are greatly complicated by the fact that the government in its discretion chooses to bring some matters as criminal and others as civil actions. Practitioners have not been able to discern any clear standard for which will be pursued in what situations. Indeed, one example illustrating the lack of clarity arises from the prosecution against Eli Lilly. A criminal case, based on the FDCA rather than the FCA, was brought against Eli Lilly in 2005 regarding alleged off-label promotions of Evista.\textsuperscript{154} Despite the consent decree and a thirty-six million dollar payment by Lilly,\textsuperscript{155} the drug was subsequently approved by the FDA for use in the treatment of breast cancer,\textsuperscript{156} the challenged off-label promotion that was the subject of the enforcement action.

The conflict the industry faces is perhaps most starkly illustrated in the case of Allergan’s Botox. Botox is an injectable biologic product used to fight wrinkles and treat abnormal muscle tone called dystonia. Allergan obtained several supplemental approvals to market the drug for different uses after its initial approval for wrinkles. But one use for which it did not have approval in the United States was the treatment of children with cerebral palsy. Physicians commonly used the drug for this and other off-label purposes. In the midst of this, the FDA ordered Allergan to heighten its warnings to reflect the serious concern for the adverse risk of “distant spread of the toxin.”\textsuperscript{157} When a drug label is revised, companies typically immediately send the revision to all physicians in the disciplines in which they believe the drug may be prescribed. But the FDA regulations do not allow Allergan to distribute the new label and warnings to doctors who were using the product off-label. Therefore, Allergan brought an action against the FDA, seeking a ruling that the regulations are unconstitutional.\textsuperscript{158} Over the same time period, the government was pursuing a case against Allergan for the off label promotion of the drug—including for treatment of migraines and cerebral palsy.\textsuperscript{159} This is notable, because Allergan had applied for approval of the drug for migraines in the United States, and it was approved in dozens of countries for treatment of cerebral palsy—but not in the United States. The multi-front battle between


\textsuperscript{155.} Id.


\textsuperscript{159.} United States v. Allergan, No. 10-cr-375 (N.D. Ga.).
Allergan and the government began in 2000, and in the fall of 2010, a global settlement was reached, with Allergan agreeing to pay $600 million and agreeing to dismiss its challenge to the constitutionality of the FDA regulations.\textsuperscript{160}

An intense battle still rages in the case of Purdue Pharma executives who were personally excluded from participation in federal health programs for twelve years after Purdue pled guilty to misdemeanor off-label promotion of the pain medication OxyContin and paid $600 million in monetary sanctions.\textsuperscript{161} In that case and in many others, the government theory is that if a company markets for an off-label purpose, then it “causes” a prescriber to file a false claim for reimbursement with Medicare, Medicaid, and other federal health care programs. This causal link is not proved or tested, because the cases settle in the main. But often, the government has evidence of a pattern of marketing by the drug representatives, accompanied by very substantial increases in the sales of the drug. This evidence, although circumstantial, is in some cases very powerful. In the case of OxyContin, a settlement was reached with the company, and certain officers entered into the misdemeanor pleas along with the company.\textsuperscript{162} The Secretary of Health and Human Services excluded the officers from participation in federal health care programs for twelve years, a substantial and unexplained departure from prior precedent.\textsuperscript{163} On appeal, the Court of Appeals for the D.C. Circuit held that the exclusion of the corporate officers was warranted on the basis of their misdemeanor misbranding convictions, but reversed and remanded the case because the Secretary of Health and Human Services’ decision as to the length of the exclusion imposed was arbitrary and capricious.\textsuperscript{164} It is widely believed that recently the government has increased its intensity and focus on the pharmaceutical company executives who allegedly enable the challenged marketing conduct, even if they do not actively engage in the conduct. Under the responsible corporate officer doctrine, this is enough for the government to pursue exclusion.

In these off-label promotion cases, it might be difficult to find individual doctors who will testify that the reason they prescribed a medication is because the drug representative told them it was safe and

\begin{itemize}
\item\textsuperscript{161} Friedman v. Sebelius, 755 F. Supp. 2d 98 (D.D.C. 2010).
\item\textsuperscript{163} Id. at *2.
\item\textsuperscript{164} Id. at *11.
\end{itemize}
effective. Indeed, we expect more from our physicians—we expect them to stay current on the scientific literature, and remain skeptical of potential scientific advances until proven with high probability. In prosecutions for off-label promotion, the government typically relies on more general evidence rather than specific proof of the basis for a specific prescription. For example, if the overall sales revenue for the drug is high for off-label uses, that may be evidence that the company was marketing it for that purpose. This was the case in the context of Neurontin sales by Warner-Lambert, which ultimately paid $430 million to resolve criminal and civil claims.\textsuperscript{165} Isolated and inflammatory testimony by a sales manager, to the effect that the company needed to sell the drug for the off-label use of pain management, weighed heavily against the company in the context of the dramatic off-label sales revenue.\textsuperscript{166} Despite the plea of Warner-Lambert to misdemeanors, the matter was automatically converted to a felony because of previous and separate convictions for FDCA violations.\textsuperscript{167} Other evidence such as business plans that depend upon growth in the off-label area, or visits by sales representatives to physicians who practice outside the area where they would be expected to prescribe the drug for the labeled purpose, are also used as proof that the company engaged in illegal marketing.\textsuperscript{168}

Despite the many prosecutions pursued, some courts have called into question whether the off-label promotion violations of the FDCA can form the basis of FCA liability.\textsuperscript{169} One court rejected the concept that pharmaceutical companies cause false claims by promoting off-label uses, stating that “the mere fact that Pfizer may have been violating FDA regulations does not translate into liability for causing a false claim to be filed . . . Pfizer did not file any claims for reimbursement and made no implied certifications to obtain payment.”\textsuperscript{170}

V. THE DOJ’S PURSUIT OF OFF-LABEL MARKETING SETTLEMENTS CREATES A DOMINO EFFECT, TRIGGERING FURTHER LIABILITIES FOR ACCUSED COMPANIES

Even if a company settles with the DOJ, the risk to the company is not over. It is not uncommon for other types of actions to follow in the wake of an off-label marketing settlement. First, state attorneys general may try to

\begin{footnotesize}
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    \item[165.] Burroughs, supra note 29, at 573.
    \item[166.] Id. at 574.
    \item[167.] Id.; see 21 U.S.C. § 333(a)(2).
    \item[168.] Burroughs, supra note 29, at 577-80.
    \item[169.] See United States ex rel Polansky v. Pfizer, No. 04-cv-0704, 2009 WL 1456582 at *7 (E.D.N.Y. May 22, 2009).
    \item[170.] Id.
  \end{itemize}
\end{footnotesize}
get in on the action, either by joining the federal action or with their own suit under a state False Claims Act or consumer fraud laws. Second, three types of private civil suits that pose the prospect of significant damages may follow. The first is a suit by patients based on state consumer fraud laws and other common law causes of action. The second is a suit by third party payors. Although their claims are sometimes included in consumer fraud class actions, they often opt out and choose to proceed with their own litigation in an attempt to recoup amounts paid for their insureds’ prescriptions of the pharmaceutical product at issue. These insurers and states bring suit on the basis that they have paid for an inflated number of prescriptions as a result of the off-label marketing or have otherwise been inappropriately charged for those prescriptions. The third is shareholder suits, which are a natural outgrowth of the type of massive expenditures needed to settle off-label marketing accusations. This ripple effect creates more costs for an accused company— costs that are likely to be passed on to consumers along with the hefty price tag of any settlement with the DOJ.

A. State Actions

With much of the investigative work already done by the DOJ and detailed in a criminal complaint or settlement agreement, state attorneys general may seek compensation on behalf of the state or its consumers. Suits by states come in several varieties. First, state consumer protection statutes may permit the attorney general to sue on behalf of the state’s consumers. The crux of these claims is that the pharmaceutical company has engaged in unfair and deceptive practices or otherwise misled consumers in violation of a state consumer fraud statute or unfair and deceptive trade practices act. Second, the attorney general may bring common law claims, such as fraud or negligence, on behalf of the state as a third party payor. These claims typically allege that, in reimbursing the prescriptions of its covered individuals, the state paid more for the drug than it would have absent the unlawful promotion of off-label uses or paid for unwarranted prescriptions of the subject drug. Third, based on similar reasoning, the state also may bring claims under a state false claims act or a state Medicaid/Medicare fraud false claims act.

Collectively, these claims can lead to substantial liability in the form of large judgments and settlements. For example, Johnson & Johnson and its subsidiaries have been the subject of a plethora of state claims over alleged off-label marketing of Risperdal and provides an example of the significant liability that may follow a DOJ allegation. In 1993, Risperdal was approved for treating schizophrenia in adults. Johnson & Johnson and its

171. See infra nn. 177-188.
subsidiaries allegedly marketed the drug for the treatment of bipolar disorder, mood and anxiety disorders, and bipolar disorder, as well as other then-unapproved uses. In 2004, the DOJ began investigating the company’s off-label promotion efforts. In 2011, the company reached an agreement in principal with the United States Attorney’s Office for the Eastern District of Pennsylvania to resolve criminal charges of a misdemeanor violation of the FDCA. In 2012, the company then reached an agreement in principle with the Department of Justice to settle three pending False Claims Act matters, two of which implicated Risperdal marketing practices. Although neither the company nor the government has announced a dollar value for these agreements, the company has taken after-tax charges of $1.7 billion to cover potential legal settlements, and The Wall Street Journal estimates that the settlement with the federal government could total as much as $2.2 billion.

During the course of the DOJ’s investigation, forty states then brought their own consumer protection or false claims suits against Johnson & Johnson or its subsidiaries over the allegedly unlawful off-label marketing of Risperdal. In 2010, claims brought by the Commonwealth of Pennsylvania in a Pennsylvania state trial court were all dismissed, including both statutory claims for submission of false and fraudulent claims and common law claims, and the nonsuit was affirmed in July 2012. In August 2012, Johnson & Johnson reached an agreement with thirty-six states and the District of Columbia to settle their claims for a combined $181 million.

In addition to these settlements, Johnson & Johnson has been hit with sizeable verdicts in several states. In Caldwell ex rel. State of Louisiana v. Janssen Pharmaceutica, Louisiana alleged that the company violated the

173. Id. at 27-28.
178. Louisiana v. Janssen Pharmaceutica, Inc. et al, Case No. 04-C-3967-D, 27th
Louisiana Medical Assistance Programs Integrity Law (“MAPIL”). In October 2010, a jury determined that the company’s marketing campaigns violated the law and awarded the state $257.7 million in civil penalties, and the company was ordered to pay $73 million in attorneys’ fees and costs. A state court of appeals affirmed the verdict, as well as the amount of the penalties, fees, and costs. In *State of South Carolina v. Janssen Pharmaceuticals*, the state claimed that the company violated South Carolina’s Unfair Trade Practices Act. In June 2011, a jury awarded the state of South Carolina $327 million in penalties, and the court denied the company’s attempts to reduce them. In June 2012, in *State of Arkansas v. Janssen Pharmaceuticals, Inc.*, the jury found that the company violated Arkansas’ Medicaid fraud law and state deceptive practices act, and the judge imposed $1.2 billion in civil penalties. Although the company is appealing these verdicts, they amount to more than $1.8 billion.

As just this one example shows, the state actions that follow in the wake of a DOJ allegation are another significant consequence of off-label marketing. Taking into account the $1.8 billion in currently-standing verdicts and the recently-agreed-to $181 million settlement, the price tag for the forty states’ claims could rival the $2.2 billion that Johnson & Johnson may pay to settle criminal and civil claims with the DOJ over its off-label marketing of Risperdal.

**B. Private Suits**

In addition to the potential for action by states, a pharmaceutical company under the scrutiny of the DOJ may face claims by the consumers

Judicial Court, St. Landry Parish, Louisiana (Oct. 15, 2010).


182. *Id.*


186. 1 Ark. J.V.R. 1, 8 (Aug. 2012).

187. *Id.*
who were prescribed the drug for an off-label purpose, by the third-party payors who paid for the drug, and by its own shareholders.

1. Suits by Consumers

Consumer fraud cases may be brought on either an individual or a class basis. Class actions typically include patients who were prescribed and purchased the pharmaceutical for an off-label purpose, but they also can include all purchasers of the drug, who allegedly paid more for it than they would have if the price had not been driven up by the off-label marketing efforts. Third party payors, as the parties who paid for the medication, may be part of the class definition in a consumer fraud class action, but they often opt out of the case to pursue claims on their own behalf. Related causes of action that may accompany a statutory consumer fraud claim include common law claims like negligence, negligent misrepresentation, fraud, civil conspiracy, and unjust enrichment.

Whether brought as an individual action or on a class basis, these claims face a number of hurdles and are often rejected at the motion to dismiss phase. First, in some jurisdictions, the “learned intermediary” doctrine bars consumer fraud claims by patients. Second, as a claim rooted in fraud, the allegations must be pleaded with particularity. As a result, the complaint must contain plaintiff-specific information and allege facts that demonstrate that either the plaintiff or his physician relied on the purported misrepresentations. It is not sufficient to rely on generic allegations about off-label marketing efforts from the criminal complaint, settlement, or other litigation, without facts showing a connection between specific illicit marketing efforts that the prescribing doctor was exposed to and the decision to prescribe the drug. Third, even when plaintiffs

188. See infra section V.B.2.

189. For example, in Smith v. Bristol-Myers Squibb Co., No. 3:06-cv-6053, 2009 WL 5216982 (D. N.J. Dec. 30, 2009), the plaintiff took Plavix in combination with aspirin as a dual therapy, an off-label use that was allegedly promoted by the defendant manufacturers and rebuffed in several letters from the FDA. After he lost sight in one eye, allegedly a result of the drug that would not have occurred if he had been taking the equally effective and less expensive aspirin-only regimen, he sued for violations of Pennsylvania’s Unfair Trade Practices and Consumer Protection Law (“UTPCPL”), 73 PA Cons. Stat. §§ 201-1, et. seq, negligence, and negligent misrepresentation. The court held that the learned intermediary operates to bar his UTPCPL claim and granted the manufacturers’ motion to dismiss. Id. at *6.

190. See, e.g., id. at *6-7 (dismissing UTPCPL claim in part because, “in the absence of specific facts in the [complaint] that Plaintiff or his prescribing physician relied upon the promotional materials that the FDA demanded Defendants discontinue disseminating four to six years prior to Plaintiff’s prescription, the Court simply cannot find that the particularity requirements have been met”).

191. See In re Schering Plough Corp. Intron/Temodar Consumer Class Action, 678 F.3d 235, 250-253 (3d Cir. 2012) (requiring plaintiff to show a connection between the
attempt to put forth evidence related specifically to their physician, they are often unable to establish the tenuous chain of causation from off-label marketing activity, to the doctor’s decision to prescribe the drug, to the plaintiff’s being injured by the drug’s being unsafe or ineffective for the prescribed condition.192

2. Suits by Third Party Payors

Like the federal government and states seeking recovery under their respective False Claims Acts, third party payors may sue over off-label marketing allegations. Third party payor claims may include statutory consumer protection or unfair and deceptive trade practices claim, claims under the Racketeer Influence and Corrupt Organizations Act (“RICO”)193 or state equivalents, common law fraud, common law unjust enrichment, and negligence. A settlement with the DOJ provides a blueprint for these suits. Although the settling pharmaceutical company is not judicially estopped from disclaiming liability in a later third party payor suit,194 the indictment and documentation of the settlement often provides much of the evidence on which the third party payor hopes to rely. While these suits are difficult for a third party payor to prevail upon, third party payor claims are not categorically frivolous195 and can lead to protracted and costly litigation.

Typically, third party payors are unable to establish that the off-label marketing caused their alleged injuries, and the claims are defeated at the motion to dismiss phase. Third party payors may point to a wide range of activities as constituting illegal off-label marketing. In In re Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation196 for instance, health insurance provider Health Care Service Corporation alleged that pharmaceutical manufacturers Pharmacia & Upjohn, Inc. and Pfizer, Inc. unlawfully marketed pain reliever Bextra for off-label uses by:

192. See, e.g., id. (dismissing claim for failure to show that the particular doctor was the subject of an illegal marketing activity and that the prescription was issued because of that activity). The court in Schering actually evaluated the two prescriptions of the pharmaceuticals at issue that were paid for by the plaintiff third party payor. For each, the court considered whether specific off-label marketing efforts or alleged bribes impacted the particular instances in which the drug was prescribed.


194. See In re Bextra and Celebrex Mktg. Sales Practices and Product Liability Litig., No. 05-CV-01699 CRB, 2012 WL 3154957, at *2, 3 (N.D. Cal. Aug. 2, 2012) (noting that, although plaintiff HCSC claimed the manufacturers should be judicially estopped from denying engagement in the alleged fraudulent behavior underlying its settlements with the government and with a class of consumers, HCSC had to meet the burden of establishing liability itself).

195. Id. at *3 (granting a motion to dismiss but stating, “[t]o be clear, the Court does not hold that a [third party payor] could never state a plausible claim for relief”).

196. Id.
(a) failing to disclose that the FDA had declined to approve Bextra for the off-label uses; (b) paying physicians to attend presentations to induce them to promote and prescribe Bextra; (c) training physicians identified as “advocates” to “serve as public relations spokespersons” for Bextra and paying them to make presentations on the drug; (d) drafting and circulating “written protocols, pain management pathways, and standing orders for Bextra” for off-label uses and dosages; (e) sending unsolicited Medical Inquiry Letters to high-volume prescribers for competitor brands; (f) distributing samples in unapproved doses to medical prescribers who had no FDA-approved use for the samples; (g) funding continuing medical education programs that were used to promote Bextra for off-label uses; and (h) sponsoring articles that promoted off-label uses.\(^{197}\)

Proving these activities actually caused the third party payor financial damage is the challenge that most cannot overcome. To have standing to assert a claim, the third party payor “must allege facts showing a causal relationship between the alleged injury – payments for [the drug] that was ineffective or unsafe for the use for which it was prescribed – and [the pharmaceutical company’s] alleged wrongful conduct.”\(^{198}\) Like consumers, third party payors must allege injury in fact and causation with specificity, and a court will evaluate claim based on the specific facts.

In Bextra, the court rejected the third party payor’s attempt to establish causation through generic theories.\(^{199}\) There, the plaintiff payor offered two theories to skirt the court’s insistence on specific allegations of causation: (1) a foreseeability theory; and (2) a “quantity effect” theory.\(^{200}\) The foreseeability theory posited that it was the foreseeable and intended consequence of the off-label marketing efforts that doctors would prescribe Bextra for unsafe, ineffective, or unapproved uses.\(^{201}\) This argument was insufficient to establish causation because it did not address the required relationship between the conduct and the harm.\(^{202}\) The “quantity effect” theory attempted to use statistics showing the extent to which sales were impacted by the off-label scheme to create an inference of causation. The third party payor reasoned that the defendants admitted that approximately sixty-five percent of Bextra sales were the result of the fraudulent off-label marketing efforts, and it had paid millions of dollars for Bextra

\(^{197}\) Id. at *1.

\(^{198}\) In re Schering Plough Corp. Intron/Temodar Consumer Class Action, 678 F.3d 235, 247 (3d Cir. 2012).

\(^{199}\) In re Bextra, 2012 WL 3154957, at *9.

\(^{200}\) Id. at *4.

\(^{201}\) Id. at *4-7.

\(^{202}\) Id. at *4, 6.
prescriptions, so some of the prescriptions it covered must have resulted from the alleged fraud. The court rejected this theory because at least some doctors were not misled by the fraudulent marketing efforts and had exercised their independent judgment. It would be impossible to know which, if any, of the prescriptions the plaintiff paid for, unless there were more specific allegations of reliance by physicians whose prescriptions were reimbursed by the plaintiff. Without specific allegations to that effect, general proof of but-for causation was impossible to establish, and the court granted the motion to dismiss for failure to sufficiently allege causation as to any of the claims.

Similarly, in July 2010, Health Care Service Corporation (“HCSC”), which operates through Blue Cross Blue Shield of several states, sued Pfizer over alleged off-label promotion of Geodon, Lyrica, and Zyvox. HCSC alleged that, as the payor for millions of health care consumers’ pharmaceutical prescriptions, it paid for an inflated number of prescriptions and related health care costs as a result of the allegedly deceptive marketing practices and inflated demand created by off-label marketing. It allegedly became aware of the marketing scheme and its injuries when the settlement with the U.S. government was announced in September 2009. Exhibits A and B to the complaint were none other than the Criminal Settlement Agreement and the Side Letter Agreement that arose out of the DOJ investigation. HCSC argued that the federal government had recovered hundreds of millions of dollars for the false claims it was forced to pay, and now the third party payors were entitled to damages for their similar losses. HCSC based its claims on the Illinois Consumer Protection Act, common law fraud, unjust enrichment, negligence and negligence per se, conspiracy, and RICO. Like the plaintiffs in Bextra, HCSC attempted to establish causation through foreseeability and quantity effect theories. The court similarly rejected both theories and held that the complaint failed to make the necessary showing of causation: it did “not contain any allegation that any doctors or other health care professional

203. Id. at *7.
204. Id.
205. Id.
206. Id. at *4, 7, 10.
208. Id. at ¶ 2.
209. Id. at ¶ 107.
210. Id. at ¶¶ 14, 67.
211. See generally id.
212. 815 Ill. Comp. Stat. § 510/2, et. seq.
relied on any Pfizer misrepresentation promoting an off-label use, as opposed to relying on the professional’s own judgment and expertise, when prescribing the drugs.”\textsuperscript{214} Although the motion to dismiss was granted, it happened only after two years of litigation and multiple motions to dismiss.\textsuperscript{215}

However, not all courts are as stringent in requiring this more particularized evidence of reliance and causation, and third party payor claims do have potential to continue past the pleading phase. In \textit{In re Actiq Sales and Marketing Practices Litigation},\textsuperscript{216} two third party payors alleged that Cephalon promoted Actiq, a drug approved for pain treatment in late stage cancer patients, for off-label use with patients with less severe conditions. As a result, the plaintiffs alleged that they had overpaid for Actiq because it had been prescribed for beneficiaries with less severe conditions who could have been treated with less expensive alternatives.\textsuperscript{217} The court did not require evidence of direct reliance by a particular physician on Cephalon’s off-label marketing statements, and the plaintiffs’ claims under Indiana and Pennsylvania consumer protection statutes survived summary judgment.\textsuperscript{218}

3. Suits by Shareholders

Shareholder suits arising from settlements that resolve allegations of FDCA violations are nothing new. Over a decade ago, in \textit{In re Abbott Laboratories Derivative Shareholder Litigation},\textsuperscript{219} shareholders alleged that Abbott’s directors breached their fiduciary duties and were liable for harm resulting from an FDA consent decree that required the company to pay a $100 million civil fine and take a number of corrective actions. Noting that the directors were aware of the violations of the law and took no steps to prevent or remedy the situation, the Seventh Circuit reversed the lower court’s dismissal and allowed the action to move forward.\textsuperscript{220}

However, the recent growth of DOJ-led investigations and high-dollar settlements has spurred the development of a cottage industry in

\begin{itemize}
\item \textsuperscript{214} See infra note 186.
\item \textsuperscript{217} See id.
\item \textsuperscript{218} Id. at *4-5.
\item \textsuperscript{219} \textit{In re Abbott Laboratories Derivative Shareholder Litigation}, 325 F.3d 795 (7th Cir. 2003).
\item \textsuperscript{220} Id.
\end{itemize}
shareholder suits against companies accused of off-label marketing. These suits can lead to large settlements, accompanied by hefty fees for plaintiffs’ counsel. For example, Pfizer’s $2.3 billion settlement with the DOJ in 2009, which resolved allegations about off-label marketing of a number of drugs, triggered the filing of several derivative suits within just a few months of the announcement. The suits were consolidated in the U.S. District Court for the Southern District of New York. The parties reached a settlement whereby Pfizer agreed to undertake additional compliance activities and to establish a $75 million fund to support a regulatory and compliance committee that would oversee its marketing practices. In April 2011, the court approved the settlement and the accompanying $22 million fee award to plaintiffs’ counsel.

More recently, following Allergan’s guilty plea and $600 million settlement with the DOJ over allegations that it illegally marketed Botox for off-label uses, the company and its directors have been faced with a bevy of derivative actions by shareholders. Plaintiff shareholders in the consolidated action In re Allergan, Inc. Shareholder Derivative Litigation in the United States District Court for the Central District of California alleged that Allergan’s directors caused the company to illegally promote Botox for off-label uses. The claims for violations of the Securities and Exchange Act of 1934, breach of fiduciary duty, corporate waste, unjust enrichment, and insider trading were ultimately dismissed based on a determination that the plaintiffs had failed to establish demand futility, as required by applicable Delaware law to pursue these claims against directors without making a prior demand to cease the offending conduct. Multiple rounds of motions to dismiss were required to reach that result.

However, even the dismissal of the consolidated federal complaint did not mean the end of the matter for Allergan and its directors. Three months after the dismissal of the consolidated federal action, the Delaware Chancery Court refused to dismiss a parallel state action, Louisiana Municipal Police Employees’ Retirement System v. Pyott, that was brought.

223. For a synopsis of Allergan’s marketing efforts, the investigation by multiple government agencies, the settlement, and the various derivative actions, see Louisiana Municipal Police Employees’ Retirement System v. Pyott, C.A. No. 5795-VCL, 46 A.3d 313, 317-22 (Del. Ch. 2012).
225. Id. at *7-12.
226. Id.
227. Id. at *2.
by other shareholders and alleged the same misconduct, but had been proceeding more slowly.\textsuperscript{228} The Delaware judge held that collateral estoppel did not apply to give the federal court’s ruling a preclusive effect against the claims of other stockholders.\textsuperscript{229} Further, the court then found that a demand would have been futile and was excused under Delaware law, thereby disagreeing with the federal court’s determination that the plaintiffs had failed to state a claim.\textsuperscript{230} The essentially identical claims of the Delaware plaintiffs were therefore allowed to continue against Allergan and its directors, despite the earlier victory against shareholders in the federal case.

Even when defendants choose not to settle shareholder suits relating to off-label marketing and are successful in defeating shareholders’ claims, that success often comes only after protracted and costly litigation. For instance, a lawsuit filed against Johnson & Johnson by the DOJ and the U.S. Attorney’s Office in Massachusetts over off-label marketing led to a protracted shareholder suit against Omnicare, Inc., a provider of pharmaceutical care services to residents at long-term care facilities.\textsuperscript{231} Relying heavily on the DOJ suit against Johnson & Johnson, the DOJ’s investigation of Johnson & Johnson, and a whistleblower suit against Omnicare, the plaintiff stock purchasers in \textit{Indiana State District Council of Laborers and Hod Carriers Pension & Welfare Fund v. Omnicare, Inc.} alleged that Omnicare and Johnson & Johnson developed a scheme to market Risperdal to nursing home patients with dementia.\textsuperscript{232} Risperdal was FDA-approved only for treatment of schizophrenia, making this an illegal off-label marketing scheme that allegedly was misrepresented in Omnicare’s registration documents, in violation of the Securities Exchange Act of 1934.\textsuperscript{233} Although the suit was ultimately dismissed, the defendant prevailed only after filing a motion to dismiss the third amended complaint and six years of litigation.\textsuperscript{234}

The trend of filing shareholder derivative suits based on DOJ allegations of off-label marketing shows no sign of slowing down. New suits continue to be filed on a regular basis, particularly after a company discloses that it has set aside hundreds of millions of dollars, or even

\begin{thebibliography}{99}
\bibitem{228} \textit{Louisiana Municipal}, 46 A.3d at 317-322.
\bibitem{229} \textit{Id.} at 323-324.
\bibitem{230} \textit{Id.} at 358-359.
\bibitem{232} \textit{Id.} at *7.
\bibitem{233} \textit{Id.} at *7-8.
\bibitem{234} \textit{Id.}
\end{thebibliography}
billion$, for potential settlements with the federal government and the state
actions that typically follow in the wake of a DOJ investigation.\textsuperscript{235}

VI. IS THE DOJ’S GOAL TO CHANGE BEHAVIOR OF PHARMACEUTICAL COMPANIES, OR TO COLLECT HUGE REVENUES FROM INDUSTRY?

It seems apparent that there is no clear public policy view that is shared
by the courts, the FDA, Congress and the health care industry on the issue
of truthful statements that might be made in the context of off-label
marketing. Indeed, one state court said exactly that in a whistleblower case
brought under an Ohio statute.\textsuperscript{236} The court noted that although the FDA
issued “Guidance” relating to off-label marketing, it had not made binding
statements of public policy: “In view of these considerations, as well as
First Amendment problems with efforts to regulate commercial speech . . .
there is no clear public policy against off-label promotion.”\textsuperscript{237} Nonetheless,
companies are faced with substantial liabilities, in the form of strong-armed
settlements with the DOJ and a bevy of associated litigation, for what is a
questionable practice at best.

One might question whether the Government’s very aggressive
enforcement actions, leading to billions of dollars in settlements on a
regular basis, have actually changed corporate conduct. Commentators
offer interesting but not totally consistent views. On one hand, Kesselheim
noted that two years after a huge settlement by Pfizer relating to Neurontin
off-label promotion, sales had actually increased by thirty-two percent and
it was estimated that over ninety percent of sales were still for off-label
uses.\textsuperscript{238} This suggested to her that the prosecution made no difference to
corporate conduct. On the other hand, Osborn believes that American drug
companies have changed behavior in the face of the challenges.\textsuperscript{239} He
describes the elimination of compensation incentives for sales
representatives based on physicians’ off-label prescribing, limits placed on
the sales representatives’ discretion to engage in discussions with
physicians beyond treatment options, and limits on the specific physicians
the representatives may visit.\textsuperscript{240}

These may be positive steps if the appropriate goal is to eliminate off-
label promotion of drugs. But if one is of the view that off-label prescribing

\begin{itemize}
\item \textsuperscript{235} E.g., Complaint, Pipefitters Local Union No. 120 Pension Fund v. White, et al.,
No. 12-cv-2624 (N.D. Ill. April 10, 2012) (following Abbott’s set aside of $1.5 billion for a
settlement related to allegations of off-label marketing of Depakote).
\item \textsuperscript{236} Long v. Rhone-Poulenc Rorer Pharm., Inc., 1999 U.S. Dist. LEXIS 14196 (N.D.
Ohio Feb. 23, 1999).
\item \textsuperscript{237} Id. at *7.
\item \textsuperscript{238} See Kesselheim, supra note 90, at 241.
\item \textsuperscript{239} Osborn, supra note 22, at 351.
\item \textsuperscript{240} Osborn, supra note 22, at 351.
\end{itemize}
is beneficial in many circumstances for patients, and that physicians are qualified to and should interpret the science independently after receiving as much information from the manufacturer as they like, then this changed conduct could be a bad result from a public health standpoint. This author concludes that if the government chooses not to stop the off-label prescription of drugs by physicians, then it has no place regulating honest dialogue pharmaceutical companies may choose to have about such uses. Indeed, in a world where many off-label prescriptions are paid for by the government knowingly and willingly in the context of Medicare and other federal programs, it is illogical to stop discussion about that prescribing practice.

Further, if other courts follow the view taken by the Second Circuit in Caronia, 241 that “truthful” speech is protected even in the context of off-label promotion of FDA-approved drugs, the government will be hard pressed to continue its prosecution of pharmaceutical companies and representatives for statements that plainly are permissible if made by any other individual. However, the critical question for government prosecutors and prospective defendants alike then becomes what constitutes a “truthful” statement about an off-label use versus a false or misleading promotion of that use. The court in Caronia cautioned that “some off-label information could certainly be misleading or unhelpful” and underscored that the case at hand did “not involve false or misleading promotion.” 242 In a footnote, the court went a step further, stating that “[o]f course, off-label promotion that is false or misleading is not entitled to First Amendment protection,” and “under 21 U.S.C. § 331(a), a defendant may be prosecuted for untruthfully promoting the off-label use of an FDA-approved drug.” 243

Absent clear guidance from the courts, where will the government draw the line between truthful statements and false or misleading promotion? For instance, simply providing a copy of a specific study that supports the use of the drug in a particular population may be dissemination of truthful information, assuming the study itself is not tainted by fraud, and protected. But would it be considered “truthful” for the representative to then characterize the use of the drug in that population as “appropriate,” particularly if there are other, contradictory findings? Proving the scientific “truth” of a statement regarding the safety or efficacy of a product used for off-label purposes might present challenges for defendants. 244 Therefore, it

242. Id. at *14.
243. Id. at *13 n.11.
244. For instance, InterMune, Inc. executive Scott Harkonen is appealing his conviction for wire fraud, a conviction that was based on issuing a press release that preliminary results of a study “demonstrated” that the company’s medication prolonged survival for patients
is far from clear that the Caronia decision, even if followed in other
Circuits, will cause the government to change course entirely or provide
reliable assurance for a pharmaceutical company that wishes to provide
information about an off-label use of its product.

Pharmaceutical company profits in recent years have appeared
enormous. Nonetheless, it is unrealistic to believe that the industry
knowingly expects to spend a huge percentage of those profits as a cost of
business pay back to the government in the settlement of fraud and abuse
lawsuits. In the end, it may be that many of these cases are settled to avoid
expensive litigation that could end in possible exclusion for both the
company and its executives, rather than due to any belief that improper
counts justifying exclusion has occurred. The costs associated with the
defense and settlement of such matters are surely passed on ultimately to
consumers of health care (and the government as provider through
Medicare, etc.) These costs may exceed any benefit realized by society
through the government’s collection of settlements and judgments.

In conclusion, two simple propositions seem apparent: 1) the
government should expressly state that it will not prosecute or attempt to
regulate the truthful communication of information about drugs between the
manufacturers and others in health care, and provide some guidance on
where it is drawing the line between truthful and false or misleading
communications regarding off-label uses; and 2) the government should
refrain from threatening the sanction of exclusion against an entire
pharmaceutical company on the basis of the alleged off-label promotion of
a single product. The threat is heavy-handed, and perhaps often
disingenuous, but it has serious consequences. It would certainly not be in
the public’s interest to have the vast majority of the companies involved in
these matters barred from supplying products for Medicare and Medicaid,
nor does the prospect of hefty penalties for dissemination of truthful
information promote the development of robust knowledge about a drug
and its potential uses.

with a rare lung disease. The government did not dispute that the study showed a higher
Survival rate for those who received the drug and that the press release accurately described
the study and its statistical findings, but the press release allegedly was fraudulent because it
opined that the data demonstrated a survival benefit. The case is United States v. Harkonen,
Nos. 11-10209 and 11-10242 (9th Cir.).
Dear Doctor Letters: Lessons in Statutory Interpretation, Preemption, Proximate Causation, and Subsequent-Remedial Measures

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I. INTRODUCTION

Dear Doctor letters (also referred to as Dear Healthcare Provider or “DHCP” letters) are an important avenue of communication between pharmaceutical manufacturers and the professionals who prescribe and administer drugs. The letters were developed as a tool for manufacturers to effectively provide healthcare professionals with key information about a drug. But how are Dear Doctor letters used by drug manufacturers in practice—to properly relay new black box warnings, or to (improperly) advertise new drug uses? Where do Dear Doctor letters fit into the FDA’s regulatory scheme—and is FDA approval required before sending out such letters (we say yes)? What impact might a Dear Doctor letter have on litigation? Could it be seen as an admission that the drug label was inadequate?

This article first discusses the applicable FDA regulations and guidance material, including the standards for when, how, and to whom Dear Doctor letters should be issued. Next, the article reviews the extent to which federal preemption principles apply to Dear Doctor letters as outlined by the Supreme Court in the landmark generic case Pliva v. Mensing. The article

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