Anomalies and Implications

The First Amendment and "Off-Label" Promotion

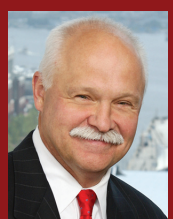
By Ralph S. Tyler, Thomasina E. Poirot, Andrea S. Andrews and Bruce R. Parker

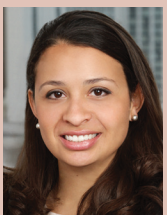
The federal government and the medical products industry have been at war over off-label promotion long enough. It is time to find a solution.

The now quite familiar headline almost screams: "Drug Company X Pays Government Many Millions [even billions] to Settle Off-Label Drug Promotion Case." Most of the media stories that accompany such headlines share certain common themes. First, the government's ability to secure a settlement means, of course, that the government extracted this large sum from Drug Company X without the government's substantiating at trial, let alone on appeal, the validity of the underlying legal theory or theories of the case, and also without the government's persuading a trier of fact that its version of the facts was more probable than whatever the company's defenses might have been.

And second, accounts of such settlements rarely assert that the settling drug company's troubles arose because the company made false or misleading statements about one of the company's drugs. Instead, Drug Company X found itself in the crosshairs because it made statements about its drug that were at odds with the drug's FDA-approved uses (indications) and FDA-approved labeling, even if the statements were factually true and not misleading. Attorneys involved in representing companies in the pharmaceutical or medical device industries, whether as in-house counsel or as outside counsel, know that truthful, non-misleading statements about uses beyond those that the FDA has approved and as stated on the label can place a company in the unenviable position of being, like Drug Company X, the target of a False Claims Act case.

The focus of this article is the First Amendment principles involved in off-label promotion cases and some of the anomalies and implications of those cases. The anomalies are striking. It is, for example, not intuitive that it is permissible, if not required as a matter of the standard of medical care, for doctors to prescribe a medication "off-label" (that is, for uses beyond those that the FDA has approved



■ Ralph S. Tyler and Bruce R. Parker are partners, and Andrea S. Andrews and Thomasina E. Poirot are associates, of Venable LLP in Baltimore. Mr. Tyler's practice concentrates on state and federal regulatory issues. He was formerly chief counsel for the FDA and held this position while the Allergan case was pending. Mr. Parker's practice emphasizes pharmaceutical and medical devices litigation. He is a past member of the DRI Board of Directors. Ms. Andrews' and Ms. Poirot's practices focus on medical products liability and toxic tort litigation.

as stated on the drug's label) while, at the same time, it is impermissible for the drug's manufacturer to promote truthfully the fact that doctors are using the drug off-label. Equally peculiar is the fact that it is entirely permissible for the doctor to promote his or her off-label use of the drug (assuming that the doctor is not connected to or compensated in any way by the drug company), but, again, the drug company is precluded from making the same promotional statements.

The Tension Between the First Amendment and the Regulation of Medical Products

An open marketplace of free expression, with a high tolerance for controversial ideas, is the core of the First Amendment. That open market First Amendment framework is at odds, however, with the tightly regulated medical product marketplace (when the term "medical products" is used in this article, it includes pharmaceuticals and medical devices). The regulated medical product marketplace has little tolerance for commercial speech promoting non-governmentally approved uses of a medical product.

The strictly enforced premise underlying the First Amendment open marketplace is that government is precluded from picking and choosing between the ideas it likes and the ones it does not. The rationale for the regulated drug product marketplace, in sharp contrast to this First Amendment model, is that only government is competent to determine which uses of a product are safe and effective (and thus approved) and, therefore, government is entitled to limit economically motivated speech to promote non-governmentally approved uses.

This clash between First Amendment and regulatory principles gets played out in its most graphic (and for industry most expensive) form because of the close and inevitable interplay between (a) the government's medical product approval/labeling scheme, (b) the government's involvement in paying billions of dollars annually for health care through Medicare and Medicaid, and (c) the False Claims Act (FCA). The government's position in FCA cases is that if the sales personnel, for example, of a medical products company promote the off-label use of one of the company's FDA-regulated products by touting truthfully off-label uses of the product and if the government pays for such off-label uses, then the government has paid a "false claim." The statutory penalties for violating the FCA are stiff. *See* 31 U.S.C. §3729 (a)(1)(g).

A fair reading of the extraordinarily rich body of First Amendment case law casts a long shadow over the government's theory in off-label promotion cases in which truthful statements trigger massive liability. As the large off-label FCA settlements confirm, however, the availability of strong defenses has seemingly made little difference to either the government or the companies it has pursued.

For the government, the incentives to bring these cases include the prospect of generating significant revenue all in the name of "fighting healthcare fraud." For industry, the incentives to settle and not to put the government's legal and factual theories to the test of full judicial scrutiny include avoiding the risk of indictment and avoiding the risk of exclusion from participation in receiving federal healthcare funds. A criminal indictment is a very heavy burden for any company, particularly a publicly traded company, and exclusion from the Medicare/Medicaid programs is effectively the economic death sentence.

There are, however, some contrary rumblings below the radar of the highly publicized settlements. These rumblings involve cases in which the relevant First Amendment-based arguments have been advanced. This article will review two of those cases. From there, we will examine how these off-label issues impact product liability tort cases. And finally, we will propose an approach that seeks to preserve the integrity of the government's drug labeling scheme while also respecting and preserving the First Amendment right of medical product companies to make truthful statements about their products.

The *Allergan* case

Allergan, Inc. v. United States, Case No. 1:09-cv-01879 (D.D.C.) ("*Allergan*"), was a civil declaratory judgment case in which the plaintiff, a pharmaceutical company, challenged FDA's prohibition of truthful, non-misleading off-label promotion of drugs. After extensive briefing of cross-motions for summary judgment, the parties agreed to dismiss the case as part of a larger settlement between Allergan and the government. The arguments in the case are nevertheless instructive.

Allergan's Allegations and Claims

Allergan's products include Botox (onabotulinumotoxinA), a product that the FDA has approved for several uses and for which FDA has approved labeling consistent with those uses. Allergan alleged that "[a]lthough many health care professionals frequently use Botox® to treat on-label conditions, *health care professionals use Botox® even more often to treat off-label conditions*." Complaint at ¶55, *Allergan, Inc. v. United States*, No. 1:09-cv-01879 (D.D.C. Oct. 1, 2009) (emphasis added). A significant example of this "more often" off-label use is treatment for "various conditions associated with spasticity, such as post-stroke spasticity in adults and lower-limb spasticity in pediatric patients with cerebral palsy." *Id.* at ¶56.

Allergan alleged that it wanted to communicate with health care professionals (not directly to consumers) medical information, including safety and dosage information, which the company had about the off-label use of Botox to treat spasticity. *Id.* at ¶¶76–86. Allergan further alleged that it was afraid of the consequences were it to engage in its contemplated "wide-ranging communication plan." *Id.* at ¶83. Specifically, Allergan alleged that "its planned truthful, non-misleading scientific speech to physicians about the use of Botox® to treat spasticity would lead to criminal prosecution and severe criminal penalties." *Id.* at ¶88.

Allergan's challenge focused on FDA's labeling and advertising regulations (21 C.F.R. §202.1). Allergan challenged as over broad and thus overly restrictive of a drug manufacturer's speech FDA's interpretation of "labeling" as encompassing all materials distributed and supplied by the manufacturer containing drug information. Allergan also challenged as facially invalid the FDA drug advertising regulation that provides that a dug is "misbranded" if an advertisement for it "suggest[s] any use that is not in the labeling accepted in [the drug's] approved new-drug application." 21 C.F.R. §202.1(e)(4)(i)(a).

The Food, Drug, and Cosmetic Act (FDCA) makes it unlawful to introduce a

drug into interstate commerce for an intended use absent FDA approval. Allergan contended that "[t]he FDCA and the FDA's regulations prohibit Allergan from speaking truthfully to health care professionals about medical issues associated with the off-label use of Botox®." Mem. Supp. Mot. Prelim. Inj. at 19, *Allergan, Inc. v. United States*, No. 1:09-cv-01879 (D.D.C. Oct. 1, 2009).

That contention is based on the way in which the statute and regulations link a drug's approval for specific "indications" (meaning uses for which the drug has been proven to be safe and effective) and drug "labeling" (which FDA interprets to include advertising). In Allergan's view, it was unconstitutionally at risk of prosecution for "misbranding" by distributing its drug if its "labeling," construing that term as Allergan alleged FDA does, contains a suggestion of off-label use or adequate directions for use.

Allergan's First Amendment analysis involved three steps: (1) FDA's rules "trigger First Amendment scrutiny because they are irretrievably content-based"; (2) "off-label promotion is protected speech because off-label use is lawful"; and (3) "although the Government has significant interests that could justify some restrictions of off-label promotional practices, there is no need for the Government to choose the drastic means reflected in FDA's regulations: the blanket suppression of off-label speech." Mem. Supp. Cross-Mot. Summ. J. and Opp. Mot. Dismiss or Summ. J. at 18–19, *Allergan, Inc. v. United States*, No. 1:09-cv-01879 (D.D.C. Jan. 15, 2010).

The Government's Response

The government's First Amendment defense largely rested on the idea that off-label promotion enjoys no First Amendment protection because the sale of a drug for an unapproved use is unlawful. *See, e.g.*, *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 563–64 (1980) ("[T]here can be no constitutional objection to the suppression of commercial messages that do not accurately inform the public about lawful activity. The government may ban forms of communication more likely to deceive the public than to inform it, or commercial speech related to illegal activity.") (citations omitted).

The government argued that Allergan's lawsuit was "a frontal assault on the framework for new drug approval" and that Allergan was seeking a regulatory regime "in which FDA's approval of a drug for one use would free the manufacturer to promote the drug for other, unapproved uses without seeking FDA approval of a drug for such other uses and without conducting adequate clinical trials to determine whether the drug is safe and effective for the unapproved uses." Mem. Supp. Mot. Summ. J. at 16, *Allergan, Inc. v. United States*, No. 1:09-cv-01879 (D.D.C. Jan. 11, 2010).

The government did not dispute that FDA treats "advertising or promotional labeling that expressly or implicitly promotes a particular use" of a drug "as evidence that the use is intended." *Id.* at 19. Further, if a drug manufacturer's "speech demonstrates, either by itself or in conjunction with the other circumstances surrounding the distribution of the drug, that an unapproved [off-label] use is an intended use, the manufacturer may not distribute the drug for that use" without obtaining FDA's approval. *Id.*

In the government's view, the lawfulness of a drug manufacturer's action turns on whether the activity is "promotional." If the manufacturer is "promoting" an unapproved off-label use of the drug, that is prohibited. If, however, the manufacturer is providing health care professionals with "non-promotional" information about the drug in an article in a medical journal, for example, that is permissible, arguably encouraged.

United States v. Caronia

United States v. Caronia, 576 F. Supp. 2d 385 (E.D.N.Y. 2008), *appeal pending* No. 09-5006 (2d Cir. 2010), is a criminal case in which the defendant pharmaceutical sales representative Caronia challenged on First Amendment grounds his indictment for violating the misbranding provisions of the FDCA as a result of allegedly promoting the off-label use of a drug (Xyrem). The district court denied Caronia's motion to dismiss the indictment in a thoughtful opinion that recognized the importance of the issues. *See id.* at 393 ("Caronia's constitutional attack calls into question America's regulatory regime for the approval and marketing of prescription drugs.").

The court in *Caronia* ruled that "promotion of off-label usage does not promote unlawful activity [and]… [p]romotion of off-label uses is not inherently misleading *simply* because the use is off-label." *Id.* at 397 (emphasis in original) (citations and quotation omitted). Nevertheless, the court denied Caronia's motion to dismiss, concluding that the government's interest in restricting a manufacturer's promotion of off-label uses is substantial, restricting promotion of off-label uses directly advances this interest, and the FDCA's restrictions are no more extensive than necessary to advance this interest. *Id.* at 398–99.

After the district court's decision in *Caronia*, but while Caronia's appeal was pending in the Second Circuit, the Supreme Court decided *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2659 (2011) ("Speech in aid of pharmaceutical marketing… is a form of expression protected by the Free Speech Clause of the First Amendment."), a case that certainly bolsters the defense's argument on appeal. *Sorrell* is discussed further below.

Off-label Claims in Product Liability Cases

The government is not alone in seeking to impose liability on medical products companies based upon claims of off-label promotion. Plaintiffs in medical products tort liability cases often make claims based on off-label promotion claims. Those claims rest on various theories, including negligence, negligence per se, breach of warranty, strict liability, misrepresentation, fraud, and unfair or deceptive trade practices.

The typical complaint alleging off-label promotion and predicating claims on those promotional statements will allege that the statements were false, untrue, misleading, or fraudulent. While a defendant may have a First Amendment defense in such a case, that defense plainly cannot be asserted successfully at the motion to dismiss stage when the allegations of the complaint are taken as true. *See Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 367 (2002) (no First Amendment protection for speech that is misleading). In such a case, the defendant would want to raise the First Amendment as an affirmative defense in its answer, conduct fact discovery to establish the truthfulness of the off-label promotional statements, and then in a motion for

summary judgment argue that the claim is barred by the First Amendment.

If a plaintiff were to allege that he or she was injured by, for example, the consumption of a drug for a prescribed off-label use and that the doctor prescribed the drug in response to a pharmaceutical sales representative's truthful, non-misleading promotional statements about the off-label use, then a First Amendment defense could be raised at the motion to dismiss stage.

Whether at the motion to dismiss stage or later in the case, the first hurdle that must be overcome is the "state action doctrine." As is well understood, the Bill of Rights, including the First Amendment, limits the powers of the federal government (and, by incorporation, the powers of state governments), not private parties; therefore, to implicate the First Amendment, there must be sufficient governmental action. There is authority for the proposition that the imposition of tort liability and filing in the state or federal judicial system is constitutionally sufficient "state action." *See In re Factor VIII or IX Concentrate Blood Prods. Litig.*, 25 F. Supp. 2d 837, 840–41 (N.D. Ill. 1998) ("The Supreme Court has established that the imposition of tort liability constitutes state action which implicates the First and Fourteenth Amendments… Nothing in plaintiff's briefs suggests that imposing tort liability would not amount to governmental action.") (citing *New York Times v. Sullivan*, 376 U.S. 254 (1964)). Assuming that the requisite "state action" nexus can be established, the question then is whether the plaintiff's claim is barred by the First Amendment.

The court will first determine if the speech is commercial, utilizing a three-factor test: (1) whether the expression is an advertisement; (2) whether it refers to a specific product and (3) whether the speaker has an economic motivation for speaking. The *Caronia* court determined that off-label promotional activities were considered to be speech. From there, the court will utilize the reminder of the *Central Hudson* balancing test to weigh the competing interests of the commercial speakers versus the government's interest in regulation. The "government interest" (here meaning the interest being advanced by the plaintiff's claim) must be substantial, the restriction imposed as a result of the plaintiff's claim must directly advance this "governmental interest," and the restriction may not be more extensive than necessary to serve that interest (*i.e.*, that there is a reasonable fit between the means and ends of the commercial speech restriction). *Thompson v. W. States Med. Ctr.*, 535 U.S. at 367 (citing *Cent. Hudson Gas & Elec. Corp.*, 447 U.S. at 566)).

The significance of the "governmental interest" will be weighed in light of the Supreme Court's analysis last Term in *Sorrell v. IMS Health, Inc.*, 131 S. Ct. 2653 (2011). In *Sorrell*, the Court invalidated a Vermont law involving the sale and use of pharmacy records. Under the Vermont law, "the information may not be sold, disclosed by pharmacies for marketing purposes, or used for marketing purposes, or used for marketing by pharmaceutical manufacturers." *Id.* at 2659. The state's conceded significant interest in protecting privacy interests and in protecting patients from prescription decisions not in the patients' best interest were not sufficient to sustain the law. The *Sorrell* Court made clear the heavy burden that the Vermont law faced and, by inference, the heavy burden of "heightened judicial scrutiny" faced by other laws restricting the speech of pharmaceutical manufacturers. *Id.* Civil tort claims based on truthful, non-misleading off label promotion claims should receive similar scrutiny, despite claims about the significance of the interests that the plaintiffs are seeking to protect.

Just as Vermont's law allowed pharmacies to share prescriber information with any entity except for marketing purposes, off-label promotion claims restrict (prohibit) pharmaceutical marketing with regard to off-label uses. The Supreme Court acknowledged that Vermont's law has the effect of preventing company sales representatives from communicating with physicians and providing them with effective information. The Court said, "the State may not seek to remove a popular but disfavored product from the marketplace by prohibiting truthful, nonmisleading advertisements that contain impressive endorsements or catchy jingles. That the State finds expression too persuasive does not permit it to quiet the speech or to burden its messengers." *Id.* at 2671.

Prohibitions of off-label promotion are defended in part on the ground that the government is protecting the health of the public by preventing biased information from entering the hands of physicians and influencing their prescribing practices. Certainly a tort plaintiff would follow this line of argument, contending that allowing off-label promotion is likely to result in bad treatment decisions because, for example, doctors will be acting in reliance upon incomplete or inaccurate information. Vermont's version of that argument in *Sorrell* did not fare well in the Supreme Court: "if pharmaceutical marketing affects treatment decisions, it does so because doctors find it persuasive. Absent circumstances far from those presented here, the fear that speech might persuade provides no lawful basis for quieting it." *Id.* at 2670.

Arguably the best case for raising a successful First Amendment defense is when the off-label use of a drug or device is common (if not the standard of care), and when the government reimburses off-label use of a drug through federally funded programs such as Medicare or Medicaid. The Medicare statute permits reimbursement for expenses that are "reasonable and necessary for the diagnosis or treatment of an illness or injury." 42 U.S.C. 1395y(a)(1)(A). The Medicare Benefit Policy Manual instructs that the Medicare contractors must determine the use to be "medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice." *Medicare Benefit Manual* 50.4.2. This manual should be consulted when defending these tort claims to determine if the product or device at issue is mandated to be reimbursed under the government's healthcare system.

Perhaps the greatest challenge in disposing of an off-label promotion claim in a tort case on First Amendment grounds is the difficulty of getting a "clean case" in which there is no factual dispute regarding the truthfulness of the allegedly offending off-label statements. That will be a rare case. The more common pattern will be that even post-discovery there will be factual ambiguity surrounding the truthfulness of the off-label statements. Were full disclosures made, for example, regarding relevant risk information? Recollections and testimony are almost certain to vary on these types of issues. In that case, the jury will be left with resolving the factual dispute and the manu-

facturer would seek a First Amendment jury instruction to the effect that if the jury finds that the off-label statements were truthful and not misleading, then the defendant is entitled to judgment on the claim.

Resolving the Conflicting and Shared Interests of the Government and Industry

What emerges from this brief review of both governmental and private off-label litigation is that litigation is unlikely to resolve these issues any time soon. Litigation is a notoriously blunt and highly imperfect instrument for resolving important policy issues. Moreover, as noted at the outset, companies have strong incentives to pay the money and settle, rather than to litigate to define more clearly the legal boundaries. That is not going to change. What needs to occur, therefore, is for the government, specifically FDA and the Department of Justice, and the medical products industry to come together with a solution, a solution that recognizes the need to protect the drug approval process while giving appropriate latitude for the exercise of First Amendment rights.

Medical products companies, both pharmaceutical companies and medical device companies, have several different types of interests that need to be reconciled. First, marketing is "protected by the Free Speech Clause of the First Amendment" and companies have an interest in marketing their products. At the same time, companies have an interest in strengthening, not undermining, the federal regulatory system. Industry's stake in a strong, credible FDA regulatory system includes being able to invoke it as evidence of safety and efficacy and as an aid in defending product liability tort suits. In addition, the FDA regulatory scheme benefits industry by promoting consumer confidence in FDA-approved products, Joseph A. Levitt, *Regulation of Dietary Supplements: FDA's Strategic Plan*, 57 Food Drug L.J. 1, 3 (2002), and FDA approval is very helpful in defending product liability lawsuits, sometimes based upon preemption and sometimes because the fact of FDA approval has a positive influence on jurors. *See* Stephanie A. Scharf *et al.*, *Juror Perceptions of the FDA That Affect Verdicts in Pharmaceutical Lawsuits*, Products Liability Litigation 43:4 (2012).

Industry also has a desire to engage in truthful off label communication, free of the threat of criminal and civil prosecution hanging over their heads. Industry has an undeniable economic incentive to engage in off-label promotion and to sell a drug for purposes other than or in addition to the one(s) for which the drug has been approved. Obtaining FDA approval for each safe and effective use is costly and the cost-benefit tradeoff is unfavorable when the potential patient population for the new (unapproved) use is small.

The federal government should likewise find the present situation highly unsatisfactory, even if it produces some revenue and occasional media stories about "fighting healthcare fraud." To begin with, a perverse consequence of the present system in which companies are at risk in false claims cases is that the Department of Justice, including United States Attorney's Offices, not FDA, is *de facto* the primary regulator of drug company conduct, particularly in the areas of advertising, promotion, and sales. Congress never intended that arrangement and the government should not want that to be the arrangement.

In addition, one part of the federal government (the Center for Medicare & Medicaid Services) is willing to pay for medically necessary and appropriate off-label uses of prescription drugs, while another agency of the same government (the Department of Justice) seeks huge sums of money from companies for promoting the same off-label's uses of the drug for which the government finds it appropriate to pay. This is a hardly orderly, let alone symmetrical, regulatory approach.

How, then, might these various interests be reconciled? First, FDA needs to abandon its present approach of distinguishing between "promotional activity" (impermissible) and "non-promotional activity" (permissible). This distinction is neither logical nor tenable. Because companies are in the business of selling their products, any statements they make potentially put them at risk for "promoting" their products.

Further, given that it is lawful and sometimes the standard of care for a physician to prescribe a drug off-label, the off-label promotion of drugs to physicians with truthful, non-misleading information should be permissible. FDA's regulations should be narrowed and clarified to make explicit that off-label promotion to physicians with truthful, non-misleading statements is permissible.

And finally, there should be statutory changes to bar criminal, civil false claim, or tort actions based upon truthful, non-misleading off-label statements about a drug when such statements are made to medical professionals. The government's legitimate interest in punishing these types of statements is doubtful, assuming it is constitutional, and such statements should not be fodder for private tort litigation.

On the other hand, the government has an altogether legitimate interest in preventing generalized off-label promotional activities being aimed at other than medical or scientific professionals. If industry were allowed to "pitch" its unapproved product wares to consumers, that would do great and ultimately irreparable damage to the drug review, approval, and labeling system. Thus, any clarification of the statutes and regulations to permit off-label promotional activities directed to medical or scientific professionals should be accompanied by counterpart rules making clear that any such promotional activities directed over the heads of medical professionals to consumers would trigger liability and carry appropriately stiff penalties.

The explosion of social media poses some special problems. Suppose, for example, a patient is, pursuant to a doctor's prescription, taking a drug off-label and that patient asks the pharmaceutical company for safety data on that off-label use. The rules need to allow latitude to permit the pharmaceutical company to respond honestly to such an inquiry without being at risk for unlawful off-label promotion of the drug.

Conclusion

The federal government and the medical products industry have been at war over off-label promotion long enough. It is time to find a solution. Government must recognize that the direction of First Amendment law is against it. The Supreme Court's decision last Term in *Sorrell* emphasizes this point. Industry, for its part, must recognize that it has too much invested in preserving the

"Off-Label", continued on page 90

"Off-Label", from page 38
reality and the perception of a strong and effective FDA regulatory system to push to the limit an absolutist First Amendment off-label promotion position. Litigation is not the answer to this problem. The answer will come through a negotiated consensus that then serves as the basis for balanced statutory and regulatory changes. FD