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White-Collar Crime

Expert Analysis

Can Truthful Statements Be a Crime? Liability for Off-Label Marketing

By **Elkan Abramowitz**

And **Jonathan Sack**

Crime in the health-care industry has been a priority of the U.S. Department of Justice for some time. The pharmaceutical industry has received particular attention, especially from federal prosecutors in Main Justice and the District of Massachusetts and Eastern District of Pennsylvania. These offices, and a handful of others, have brought a series of high-profile prosecutions, resulting in corporate guilty pleas and billions of dollars of criminal fines and civil penalties for unlawful "off-label" marketing of prescription drugs—a theory of criminal liability derived from the Food, Drug and Cosmetic Act (FDCA).

When a pharmaceutical company sells a prescription drug, it must first receive approval from the Food and Drug Administration (FDA). The approval of a drug is for a particular medical condition and patient population, and that approval is incorporated in a package insert, or "label"—what consumers may see as the small-print, multi-fold paper inserted into a package that contains the drug. Prescription drugs are often approved for one use, but prescribed by doctors in unapproved doses and for unapproved medical conditions or types of patients.[1]

The marketing and promotion of drugs off-label occurs when a pharmaceutical company seeks to persuade doctors to use drugs for conditions not approved on the label.[2] While off-label prescribing is lawful and sometimes ethically necessary for treatment,[3] the FDA and Justice Department have treated off-label marketing of drugs by pharmaceutical companies as a serious criminal offense—an effort to evade an important regulatory regime and sell drugs in a potentially dangerous manner. Significantly, the FDA and Justice Department have viewed off-label marketing as a serious crime even when the marketing efforts rested on accurate and truthful information.

Notwithstanding the guilty pleas by companies and billions of dollars in payments to the government, serious questions about the justification for criminal liability for such off-label marketing have arisen. The few prosecutions for off-label marketing that resulted in contested cases and trials have generally not been successful for the government, yielding dismissals and reversals on appeal.[4]

> In 'Amarin Pharma,' the court held that prosecutions for truthful off-label marketing violated the First Amendment's protection of commercial speech.

More fundamentally, the U.S. Court of Appeals for the Second Circuit held in *United States v. Caronia*[5] in 2012 that a prosecution based on truthful statements violated the First Amendment protection of commercial speech as articulated by the Supreme Court in recent years, and vacated the conviction of a pharmaceutical company employee for off-label promotion.[6] The Justice Department construed the decision quite narrowly, however, as reflected in a guilty plea by biotechnology company Amgen 16 days after the Caronia decision was issued.

Into this controversy now comes a decision from Southern District of New York Judge Paul A. Engelmayer, issued Aug. 7, 2015, which thoroughly considered the impact of *Caronia* on criminal liability for truthful off-label marketing of prescription drugs. In *Amarin Pharma v. FDA*,[7] a lawsuit seeking to enjoin the FDA from implementing the FDCA in a manner that had a chilling effect on free expression, the court held that prosecutions for truthful off-label marketing violated the First Amendment's protection of commercial speech, thus giving *Caronia* the broad reading previously sought by the pharmaceutical industry and rejected by the government.

Off-label marketing as a theory of criminal liability bears similarity to other doctrines of white-collar crime, such as honest services fraud based on undisclosed conflicts of interest. Such doctrines serve as a basis for highly assertive prosecutions until a court steps in to articulate clearly how the government may have overstepped legal bounds.

Holding in 'Amarin Pharma'

In 2012, Amarin received FDA approval to market its drug, Vascepa, to treat adult patients with triglyceride levels above 500 mg/dL (milligrams per deciliter), referred to as "very high triglycerides." Amarin also sought but did not get FDA approval to market the drug for patients with triglyceride levels between 200 and 499 mg/dL, referred to as "persistently high triglycerides." While the use of Vascepa can safely and effectively reduce triglyceride levels in this second group of patients, the FDA concluded that it was unclear whether lower triglyceride levels in this group of patients also reduces cardiovascular risk. As a result, any marketing of Vascepa for patients with persistently high triglycerides would be "off-label."

In its final response to Amarin's proposal, the FDA told the company that the drug "may be considered to be misbranded under the [FDCA] if it is marketed" for patients other than those with

ELKAN ABRAMOWITZ *and* JONATHAN SACK *are members of Morvillo Abramowitz Grand Iason & Anello P.C.* GRETCHAN R. OHLIG, *an attorney, assisted in the preparation of this article.*

very high triglycerides. Despite the FDA's statement, Amarin wanted to market Vascepa based on studies that demonstrated the reduction of triglyceride levels in patients with persistently high triglyceride levels. In the face of the FDA's explicit "threat" to bring a misbranding action if it did so, Amarin filed suit, seeking injunctive relief and a declaratory judgment that the FDA's prohibition on "off-label" promotion, as applied to truthful and non-misleading speech, was unconstitutional under the First Amendment.[8]

In the FDA's view a drug manufacturer that markets or promotes a drug for an unapproved use violates the FDCA. While the FDCA and accompanying regulations do not expressly prohibit the promotion or marketing of drugs for off-label use, the statute prohibits the introduction into interstate commerce of any drug that is misbranded. Misbranded drugs have been considered to include those with labeling that does not bear "adequate directions for use" pursuant to which a consumer can "use a drug safely and for the purposes for which it is intended."[9] "Intended use" is defined by reference to "the objective intent of the persons legally responsible for the labeling of drugs," which may be proven by "oral or written statements by such persons or their representatives."[10]

The Justice Department has relied on these provisions to prosecute drug manufacturers and their employees for affirmatively marketing and promoting off-label uses of prescription drugs, arguing that statements made pursuant to these efforts establish unlawful conduct and an "intended use" that is not adequately set forth on the drug's label. In the government's view, such behavior constitutes a misdemeanor, irrespective of the truth or falsity of the information conveyed, or felony charges for fraudulent misbranding if the information conveyed is false or misleading.[11]

The FDA tried to render its dispute with Amarin moot by agreeing to permit the company to make certain statements regarding off-label uses of Vascepa. Amarin rejected the FDA's efforts and brought suit. In its opposition to the company's application for preliminary relief, the FDA argued that Amarin's attempt to make proactive statements to doctors regarding the use of Vascepa for patients with persistently high triglycerides was "a frontal assault…on the framework for new drug approval that Congress created."

In evaluating Amarin's petition and the likelihood of success on the merits, Judge Engelmayer focused on the parties' conflicting readings of the Caronia decision. In *Caronia*, the Second Circuit vacated the misdemeanor misbranding conviction of Alfred Caronia, a pharmaceutical sales representative who promoted off-label uses of Xyrem, a prescription narcolepsy drug. The FDA acknowledged that the comments made by Caronia to doctors about Xyrem's off-label uses had been truthful.

The Second Circuit held that truthful and non-misleading off-label promotional speech is constitutionally protected under the First Amendment and, as a corollary, that off-label promotional speech would not constitute a criminal offense unless the speech was false or misleading. The court observed that "[t]he government's construction of the FDCA essentially legalizes the outcome—off-label use—but prohibits the free flow of information that would inform that outcome."[12]

The FDA and Justice Department read *Caronia* narrowly, as suggested by cases brought following the Second Circuit's decision.[13] The FDA contended that *Caronia* was limited to its particular facts and insisted that it retained "the ability to bring a misbranding action where the conduct at issue consists solely of truthful and non-misleading speech promoting an off-label use of an approved drug."[14]

Closely analyzing the Caronia decision in light of the Supreme Court's recent commercial speech jurisprudence, Judge Engelmayer expressed his "considered and firm view…that, under *Caronia*, the FDA may *not* bring [a misbranding] action based on truthful promotional speech alone, consistent with the First Amendment."[15] Accordingly, *Amarin* sufficiently established a substantial likelihood of success on the merits.

In reaching this conclusion, Engelmayer rejected the FDA's attempt to analogize misbranding to the crimes of jury tampering, blackmail and insider trading in which "the speech is the act." In contrast, the court held, truthful and non-misleading speech promoting the off-label use of an FDA-approved drug "*cannot* be the act upon which the action is based."[16] While truthful speech may be admitted to establish a party's intent, or mens rea, for example when the misconduct consisted of "non-communicative activities," truthful speech may not be the basis for proving the unlawful act of misbranding, or actus reus, of the conduct at issue.[17] Further, as Engelmayer observed, *Caronia* left room for the prosecution of off-label marketing as misbranding when the speech was misleading or false. "In the end, however, if the speech at issue is found truthful and non-misleading, under *Caronia*, it may not serve as the basis for a misbranding action."[18]

Conclusion

If Judge Engelmayer's interpretation of *Caronia* becomes authoritative, it will end reliance on a doctrine of criminal liability that the Justice Department has used to fight claimed corporate wrongdoing. It will also put to rest a theory of white-collar criminal conduct that had long been questioned by commentators and industry advocates but rarely litigated.

Other expansive theories of white-collar liability have suffered a similar fate—e.g., honest services fraud before the enactment of Section 1346 of Title 18,[19] honest services fraud based on undisclosed conflicts of interest before *Skilling v. United States*,[20] certain structuring offenses before the decision in *Ratzlaf v. United States*,[21] and most recently theories of remote tippee liability before the *United States v. Newman* decision.[22]

Of course, we do not know the ultimate effect of the Amarin Pharma and Newman decisions; that will depend on government appeals and further case law. What we know is that checks and balances, the process of seeking to limit as well as expand theories of white-collar criminal liability, remain vital to a healthy system of justice.

1. According to recent reports, about one of five prescriptions written in the United States are for non-FDA-sanctioned uses. "Off-label use is vital for complex conditions like cancer and psychiatric disorders that require trial and error for individual patients, who can't wait years for the FDA's blessing." Opinion, "A Free Speech Clinic for the FDA," The Wall Street Journal (Aug. 14, 2015). See also *Amarin Pharma v. FDA*, 2015 WL 4720039, *3 (S.D.N.Y. Aug. 7, 2015) ("In certain fields, off-label prescription is the norm rather than the exception.").
2. In contrast to affirmative efforts to market products off-label, pharmaceutical companies are permitted to respond to physician inquiries about possible off-label uses. The FDA has recommended certain limited methods for responding to such inquiries. *Amarin Pharma*, 2015 WL 4720049 at **6-7.
3. Id. at *3-4.
4. See e.g. David Voreacos, "Stryker President's Criminal Charges Dropped by Prosecutors," Bloomberg (Feb. 2, 2012); *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012). See also Alicia Mundy and Brent Kendall, "U.S. Rebuffed in Glaxo Misconduct Case," The Wall Street Journal (May 11, 2011) (dismissal of obstruction charges arising out of off-label case); Shelley Murphy and Alice Dembner, "All Acquitted in Drug Kickbacks Case: Jury Deals a Blow to US Prosecutors," The Boston Globe (July 15, 2004).
5. 703 F.3d 149.
6. See Jonathan Sack, "Does Misdemeanor Misbranding Survive *Caronia*?" The Insider Blog, Forbes.com (Dec. 11, 2012).
7. 2015 WL 4720039 (S.D.N.Y. Aug. 7, 2015).
8. Id. at *13.
9. 21 U.S.C. §§331(a); 352(f). 21 C.F.R. §201.5.
10. 21 C.F.R. §201.128.
11. See *Caronia*, 703 F.3d at 154.
12. Id. at 167.
13. See Robert Radick, "Caronia and the First Amendment Defense to Off-Label Marketing: A Six Month Re-Assessment," The Insider Blog, Forbes.com (May 29, 2013).
14. 2015 WL 4720039 at *8.
15. Id. at *23 (emphasis in original).
16. Id. at *25 (emphasis in original).
17. Id. at *22, 26-27.
18. Id. at *27.
19. *McNally v. United States*, 483 U.S. 350 (1987).
20. 561 U.S. 358 (2010).
21. 510 U.S. 135 (1994).
22. 773 F.3d 438 (2d Cir. 2014).