

A NEW WEAPON IN PHARMA CASES

Pharmaceutical companies that market off-label uses for FDA-approved drugs may weave a tangled web of half-truths, omissions, and outright lies to increase their bottom lines. As a result, drug purchasers, such as health insurers and consumers, may be injured by paying for worthless and possibly dangerous drugs.

The Federal Food, Drug, and Cosmetic Act (FDCA) forbids drug marketing for off-label uses but does not create a private right of action. Drug purchasers harmed by off-label promotion must use another avenue to obtain redress.

A newly proven method of recovery is a fraud-based civil claim under the Racketeer Influenced and Corrupt Organizations Act (RICO). In a multi-district litigation case decided last year, one plaintiff, Kaiser Foundation Health Plan, achieved a favorable jury verdict against Pfizer for its off-label marketing of the anti-epileptic drug Neurontin.¹

At trial, Kaiser showed that it based its prescription drug formulary restrictions of Neurontin on Pfizer's fraudulent, off-label marketing activities, which included direct marketing to physicians; sponsorship of educational events attended by physicians; and the suppression of negative clinical trial results about the drug's efficacy at higher than approved doses and for the off-label treatment of bipolar disorder, neuropathic pain, and migraines. Kaiser spent more than \$100 million on Neurontin over a 10-year period when it could have paid for less expensive alternatives.

A successful civil RICO case against one pharmaceutical giant may be the key to holding others accountable for injuries caused by off-label drug uses.

By || **THOMAS M. GREENE**



As the Kaiser case illustrates, a civil RICO claim must allege that the defendant engaged in an enterprise through a pattern of racketeering activity.² Plaintiffs also must prove a direct relationship between the injury and alleged injurious conduct.³ Obstacles include establishing a pattern of racketeering activity by certain predicate acts, satisfying the enterprise element of the statute, and proving that the racketeering conduct caused the plaintiffs' injuries. In addition, plaintiffs alleging fraud must state with particularity the circumstances constituting fraud.⁴

Proving Predicate Acts

The racketeering activity required as an element of a civil RICO claim "consists of no more and no less than the commission of a predicate act."⁵ Two or more predicate acts are required to establish a pattern.⁶ To constitute a pattern, the predicate acts must have been continuous, meaning committed within 10 years of each other. They also may not stem from a single act. For example, sending a physician the same fraudulent letter by post and e-mail could be considered both mail and wire fraud, but it doesn't on its own establish a pattern of racketeering activity.⁷

It may not be difficult to meet the pattern requirement in a pharmaceutical case like the one against Pfizer because off-label marketing campaigns typically feature numerous efforts to communicate with physicians. Proving that the drug company engaged in racketeering activity, however, is more challenging. Absent from the exhaustive list of predicate acts for a civil RICO claim are violations of the FDCA.⁸

A drug company's misrepresentation of the benefits and risks of its drugs could be considered mail or wire fraud. Such misrepresentations may be especially likely for off-label indications because drug companies with conclusive evidence that a drug is safe and effective for a claimed use have strong incentive to petition the FDA to amend the drug's labeled indications.

Drug companies use several techniques to mislead the medical community about a drug's effectiveness for off-label indications. The most pernicious is simply failing to publish negative studies.

Studies showing that a drug does not work for a particular condition can be just as important to clinicians as those that prove its effectiveness. If a drug

company publishes only studies with favorable results, the medical community has no way of knowing that the results are dubious. Scientists call this phenomenon "selective outcome reporting" bias.⁹ But to the legal community, it's fraud.¹⁰

Drug companies, with the assistance of medical marketing firms, may also cause medical articles to be published that do not accurately describe study results. For example, they may change the primary endpoint—the study's main outcome—after reviewing the results of a clinical trial, so what would have been a negative trial under the original protocol is presented as a positive trial.

Another technique for turning nega-



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tive trial results into positive results is redefining the population to be studied after the findings are available. By eliminating patients with negative results from the study sample, statistical significance can be achieved after the fact. Some medical articles do not disclose these techniques of manipulation, or “moving the goalposts.”

When Kaiser’s expert compared the published medical articles for Neurontin to the original protocols and internal research reports, she found that each one exhibited “some form of bias or deviation from the truth.”¹¹ Pfizer’s repeated and intentional misreporting of medical research was the predicate act needed to claim mail and wire fraud.¹²

Establishing an Enterprise

A successful RICO claim requires proof that the defendant participated in an enterprise, defined as “any individual, partnership, corporation, association, or other legal entity, and any union or group of individuals associated in fact although not a legal entity.”¹³

The U.S. Supreme Court has broadly construed the requirement, ruling that an enterprise must be a group of persons associated for the common purpose of engaging in a course of conduct.¹⁴ An enterprise thus includes any union or group of individuals associated in fact—which can be proven by evidence of an ongoing organization, formal or informal—with the various associates functioning as a continuing unit.¹⁵

Even if some participants in a publication enterprise are unaware that medical journal articles and other communications about off-label indications are fraudulent or misleading, they all may be aware that they are assisting in the off-label marketing of a drug, which is illegal. So although their conduct may be distinguished from the fraud required

in a RICO case, an association-in-fact that has a purpose of furthering off-label marketing is an illegal common purpose.¹⁶

Mere conspiracy is not enough to establish an enterprise; the activity must be more than an ad hoc, one-time criminal venture.¹⁷ There must be an ongoing structure or series of relationships that allows the enterprise to continue to operate over time.

Kaiser successfully alleged that a drug company and a medical marketing firm could form an enterprise. Kaiser then argued and offered evidence at trial that Pfizer’s association with each of two marketing firms was an enterprise.

Each of these firms had worked with Pfizer over a period of years to create tactical plans to promote Neurontin off label. Each was in regular communication with Pfizer in pursuit of that end, and Pfizer compensated the firms for their involvement. The length of the companies’ joint marketing efforts demonstrated that the relationships were ongoing, rather than ad hoc.

Clinching Causation

Predicate acts and a viable enterprise alone are not sufficient proof to win a RICO case. Plaintiffs must have been injured by the defendant’s racketeering activity. Proof of causation in these cases is challenging because off-label marketing is generally directed toward physicians, not the consumers or health plans who pay for the prescriptions.


The Supreme Court has made it clear that plaintiffs are not required to prove that they relied on a defendant’s false representations to prevail in a fraud-based civil RICO claim.¹⁸ Still, plaintiffs must prove that they were injured by the defendant’s fraudulent conduct. As a practical matter, they will be unable to establish “but for” causation unless they show that the defendant’s misrepresentations or omissions affected another’s

conduct to their detriment.¹⁹

In the Neurontin litigation, health insurers and other prescription drug purchasers, including Kaiser, presented aggregate economic data showing that Pfizer's fraudulent marketing campaign greatly increased the number of off-label prescriptions by physicians. The court acknowledged that this evidence established that the marketing campaign "likely caused [the plaintiffs'] injury."²⁰

But the court also found that the plaintiffs had provided insufficient evidence to determine which physicians had relied on the fraudulent representations. The court required the plaintiffs to present direct evidence that their insurance plans relied on those representations or omissions, or to provide a reliable methodology to calculate an accurate percentage of doctors who relied on the fraudulent communications.

Kaiser met this burden in two ways. First, it proved that the medical literature about Neurontin, on which the health plan relied in deciding to relax its restrictions on off-label use imposed on participating doctors, was misleading. Second, Kaiser showed that Pfizer, through direct communications with doctors that misrepresented the drug's efficacy, thwarted its later attempts to restrict rampant off-label use.²¹

RICO's powerful remedies make it an attractive tool to redress fraud injuries, but its onerous requirements often prevent plaintiffs from pursuing claims. Fraudulent off-label marketing is one area where RICO can be applied successfully. However, evidence of loss causation must be carefully assembled so plaintiffs can prove that they would not have reimbursed claims for off-label use had the drug company properly disclosed the complete medical evidence. 

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NOTES

1. *Kaiser Found. Health Plan, Inc. v. Pfizer, Inc.*, No. 04-CV-10739 (D. Mass. Mar. 25, 2010). The case was also tried under California’s Unfair Competition Law, *In re Neurontin Mktg. & Sales Prac. Litig. (Neurontin III)*, 748 F. Supp. 2d 34 (D. Mass. 2010).
2. 18 U.S.C. §1962(c) (2006); see *Sedima, S.P.R.L. v. Imrex Co.*, 473 U.S. 479, 496 (1985).
3. *Holmes v. Secs. Investor Protec. Corp.*, 503 U.S. 258, 268 (1992).
4. Fed. R. Civ. P. 9(b); *Am. Dental Assn. v. Cigna Corp.*, 605 F.3d 1283, 1291 (11th Cir. 2010).
5. *Sedima*, 473 U.S. at 495.
6. 18 U.S.C. §1961(5) (2006).
7. *Id.*; see *H.J. Inc. v. Nw. Bell Tel. Co.*, 492 U.S. 229 (1989); *Sedima*, 473 U.S. at 496 n. 14.
8. See 18 U.S.C. §1961(1) (2006).
9. *Neurontin III*, 748 F. Supp. 2d at 44.
10. *Id.* at 82–83.
11. *Id.* at 43–44.
12. *In re Neurontin Mktg. & Sales Prac. Litig. (Neurontin II)*, 677 F. Supp. 2d 479, 492 (D. Mass. 2010).
13. 18 U.S.C. §1961(4) (2006).
14. See *Sedima*, 473 U.S. at 496; *U.S. v. Turkette*, 452 U.S. 576, 583 (1981).
15. See *Turkette*, 452 U.S. at 580, 583.
16. See *In re Neurontin Mktg. & Sales Prac. Litig. (Neurontin I)*, 433 F. Supp. 2d 172, 180 (D. Mass. 2006).
17. See *U.S. v. Cianci*, 378 F.3d 71, 82 (1st Cir. 2004); *Fitzgerald v. Chrysler Corp.*, 116 F.3d 225, 228 (7th Cir. 1997).
18. *Bridge v. Phoenix Bond & Indem. Co.*, 553 U.S. 639, 661 (2008).
19. *Id.* at 658–59.
20. *Neurontin II*, 677 F. Supp. 2d at 495.
21. *Id.* at 496–97; *Neurontin III*, 748 F. Supp. 2d at 63–65.