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Off-Label Drug Marketing, the First Amendment, and Federalism

David Orentlicher*

INTRODUCTION

For decades, the government has tried to promote the public's health by regulating the flow of information from physicians, drug companies, and other persons or businesses to consumers and patients.¹ The federal government requires the familiar nutrition labels on baked items, canned goods, and other processed foods;² it also requires cigarette manufacturers to apprise potential purchasers about the risks from smoking.³ And states generally require physicians to discuss risks, benefits, and other information about a patient's therapeutic options as part of the informed consent process.⁴

In addition to mandating certain disclosures of information to promote health, the government prohibits other disclosures of information that it deems harmful to health. For example, the United States Food and Drug Administration (FDA) restricts the freedom of

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1. The government also tries to promote the public's health by disseminating information directly to individuals, as with the U.S. Department of Agriculture's food pyramid in the past and food plate now. *See generally* Donald K. Layman, *Eating Patterns, Diet Quality and Energy Balance: A Perspective About Applications and Future Directions for the Food Industry*, 134 *PHYSIOLOGY & BEHAV.* 126, 127–28 (2014).

2. 21 U.S.C. § 343(q) (2012). More recently, the federal government has mandated calorie disclosures on restaurant menus. David Orentlicher, *Health Care Reform and Efforts to Encourage Healthy Choices by Individuals*, 92 *N.C. L. REV.* 1637, 1642–48 (2014) (discussing 21 U.S.C. § 343(q)(5)(H) (2012)).

3. 15 U.S.C. § 1333 (2012).

4. Many states also mandate specific disclosures by physicians as part of the informed consent process. This is common when informed consent is obtained from patients before an abortion or treatment for breast cancer. David Orentlicher, *Abortion and Compelled Physician Speech*, 43 *J.L. MED. & ETHICS* 9, 10–11 (2015).

pharmaceutical companies to advertise “off-label” uses of their drugs.⁵ The FDA also limits the ability of food manufacturers to promote the ways in which their products might improve health or treat disease.⁶

But what may be good for health may not be constitutional. The First Amendment rightly recognizes that people generally must be able to speak freely without the government telling them what to say or what not to say. A robust free market of speech provides a critical safeguard for individual liberty. In short, government regulation of health-related information can bring two fundamental interests into conflict—the public interest in good health and the public interest in free speech. How, then, should the courts draw a balance between these two critical interests?

In this Article, I consider the FDA’s restrictions on off-label promotional speech by pharmaceutical companies. As mentioned,⁷ the FDA limits the freedom of companies to market their drugs for off-label uses—even though physicians are free to prescribe the drugs for those uses. By conditioning the freedom to advertise on whether a promoted use has been approved for inclusion on the drug’s label, the FDA gives pharmaceutical companies a strong incentive to

5. Off-label use refers to the fact that when the FDA approves a drug, it approves the drug for a specific use (or uses). Ralph F. Hall & Elizabeth S. Sobotka, *Inconsistent Government Policies: Why FDA Off-Label Regulation Cannot Survive First Amendment Review Under Greater New Orleans*, 62 *FOOD & DRUG L.J.* 1, 4 (2007). For example, when the FDA first approved Botox (now widely used with FDA approval for cosmetic purposes), the agency approved the drug for the treatment of two eye problems, strabismus and blepharospasm. Coleen Klasmeier & Martin Redish, *Off-Label Prescription Advertising, the FDA and the First Amendment: A Study in the Values of Commercial Speech Protection*, 37 *AM. J.L. & MED.* 315, 329 (2011). Once a drug is approved, the package insert for the drug describes the approved use or uses (the “on-label” uses). On-label uses include not only the diseases which the drug can treat, but also whether the drug is approved for use in children as well as adults, and the dose at which the drug should be prescribed. Hall & Sobotka, *supra*, at 5. Once a drug is prescribed for approved uses, physicians may recognize other valuable uses for the drug. Hence, physicians are free to prescribe drugs for any medically justified purpose even if the use has not been approved by the FDA (off-label uses). John E. Osborn, *Can I Tell You the Truth? A Comparative Perspective on Regulating Off-Label Scientific and Medical Information*, 10 *YALE J. HEALTH POL’Y L. & ETHICS* 299, 303 & n.5 (2010). While physicians are free to prescribe the drug for off-label uses, pharmaceutical companies are not free to promote the off-label uses.

6. Hilary G. Buttrick & Courtney Droms Hatch, *Pomegranate Juice Can Do That? Navigating the Jurisdictional Landscape of Food Health Claim Regulation in a Post-POM Wonderful World*, 49 *IND. L. REV.* 267 (2016).

7. See *supra* text pp.89–90.

demonstrate that their drugs are indeed safe and effective for new uses.⁸ At the same time, physicians need not wait for approval before prescribing the drug for new uses if preliminary medical evidence suggests that the drug is safe and effective for those uses. By treating drug company promotion differently from physician prescribing, the FDA tries to draw an appropriate balance between access to effective uses of drugs and protection from unsafe uses of drugs.

And we know from experience that patients gain important benefits from some off-label uses while realizing no benefit or even harm from other off-label uses. For example, among important treatments for cancer, off-label uses of drugs are common.⁹ In these cases, off-label prescribing provides significant benefits. In other cases, off-label uses are harmful. For example, when physicians routinely prescribed hormone replacement therapy off label to postmenopausal women in the 1980s, the women were exposed to an increased risk of breast cancer, heart attack, and stroke.¹⁰ Overall, the likelihood of adverse side effects is greater with off-label uses of drugs than with their on-label uses.¹¹ By restricting the promotion of off-label uses, the FDA can limit the extent to which drugs are prescribed for off-label uses until data on safety and effectiveness provide a clearer picture of a drug's value for a new use.

In recent years, especially in the wake of the decision by the U.S. Court of Appeals for the Second Circuit in *United States v. Caronia*,¹² the FDA's authority to regulate off-label promotional speech has been called into question. According to the *Caronia* court, the FDA's rules run afoul of the First Amendment's freedom of speech. In the court's view, the FDA's regulations create a conflict between government power and the safeguards provided by the First Amendment against an overreaching state, and the government's desire to regulate must yield to the Constitution's interest in personal

8. Aaron S. Kesselheim, *Off-Label Drug Use and Promotion: Balancing Public Health Goals and Commercial Speech*, 37 AM. J.L. & MED. 225, 239 (2011).

9. Hall & Sobotka, *supra* note 5, at 7; Kesselheim, *supra* note 8, at 235.

10. Christopher Robertson, *When Truth Cannot Be Presumed: The Regulation of Drug Promotion Under an Expanding First Amendment*, 94 B.U. L. REV. 545, 561 (2014).

11. Tewodros Eguale et al., *Association of Off-Label Drug Use and Adverse Drug Events in an Adult Population*, 176 JAMA INTERNAL MED. 55 (2016)

12. 703 F.3d 149 (2d Cir. 2012).

liberty. If the FDA wants to limit off-label uses of drugs, it can regulate those uses directly rather than regulating them indirectly through the suppression of promotional speech.¹³

However, direct regulation of off-label use raises its own constitutional concerns. Limits on off-label prescribing also implicate a fundamental constitutional principle that is designed to safeguard individual liberty—the principle of federalism. Restricting off-label use rather than off-label promotion may allow the FDA to avoid First Amendment problems, but it forces the FDA to intrude into matters traditionally regulated by state governments—it is state legislatures and licensing boards, rather than the federal government, that oversee doctors as they practice their craft, including decisions about treatment options for their patients.¹⁴ In other words, when it comes to the regulation of off-label uses of drugs, federalism is just as much at stake as is freedom of speech. Because of the FDA’s desire to respect state government authority, together with other considerations discussed in this essay, courts should reject the analysis of the *Caronia* court and give the FDA significant leeway in its regulation of off-label marketing.

I. BACKGROUND

Although the federal government allows physicians to exercise their medical judgment in deciding whether to *prescribe* a drug for a particular purpose, it does not allow pharmaceutical companies the same freedom to decide whether to *promote* a drug for a particular purpose. In its regulation of pharmaceutical company marketing activities, the FDA distinguishes between the promotion of on-label uses and the promotion of off-label uses.

13. *Id.* at 168.

14. Of course, regulation of medical practice is much more nuanced. The federal government often influences the practice of medicine through the conditions it attaches to reimbursement for care under Medicare or Medicaid (notwithstanding the Medicare statute itself which states that it shall not “be construed to authorize any Federal officer or employee to exercise any supervision or control over the practice of medicine or the manner in which medical services are provided,” 42 U.S.C. § 1395 (2012)). But federal authority is stronger when Congress exercises its spending power than when it exercises its commerce clause power, the main authority for federal regulation.

Under federal law, it is a crime to introduce a prescription drug into interstate commerce if the drug is “misbranded.”¹⁵ A drug can be misbranded in a number of ways. For purposes of off-label marketing, a drug is misbranded if its labeling does not include adequate directions for its intended uses,¹⁶ which is necessarily the case for off-label uses, since there are no directions on the label for those uses.

Of course, when a pharmaceutical company sells its drugs, it can intend that they be used for on-label uses, so how does the government demonstrate that off-label uses were intended and that the drugs are misbranded? The FDA can cite to pharmaceutical marketing materials or other promotional speech as evidence of the company’s intent. If a company promotes off-label uses, then that is strong evidence that the company intends those uses.¹⁷ In the government’s view, companies are not prosecuted merely for promoting their drugs—a criminalization of speech—but for selling misbranded drugs—a criminalization of conduct. And of course, the government often uses a defendant’s speech as evidence of the defendant’s intent to commit a crime, as in conspiracy or fraud cases.¹⁸

In the *Caronia* case, the court addressed the FDA’s misbranding theory in a muddled way, leaving some uncertainty about the application of its decision in other cases. Initially, the court concluded that Alfred Caronia was not in fact convicted because of misbranding; rather, he was convicted because of his speech (i.e., his discussions with physicians about off-label uses of his company’s drugs). According to the court, the FDA presented a case against Mr. Caronia for his words rather than for his company’s misbranding. Under this view of *Caronia*, the FDA can still prosecute pharmaceutical company executives when they promote off-label uses, as long as the agency is careful about the way it formulates its case. And it is not surprising that the Second Circuit was skeptical

15. 21 U.S.C. § 331(a) (2012); 21 U.S.C. § 333(a) (2012).

16. 21 U.S.C. § 352(f) (2012).

17. *Caronia*, 703 F.3d at 160–61.

18. KENT GREENAWALT, *SPEECH, CRIME, AND THE USES OF LANGUAGE* 80–81, 132–33 (1992).

about the FDA's case against Mr. Caronia. He was not a senior executive who oversaw company sales. Rather, he was a sales representative who discussed off-label uses with physicians who might prescribe his company's drugs.¹⁹ Mr. Caronia was not introducing the drugs into interstate commerce; his superiors were doing so.

But the Second Circuit's opinion also discussed the First Amendment problems with FDA's off-label marketing regulations in a broader context and indicated that they would not pass muster even if prosecutions were properly characterized as misbranding cases and brought against senior company executives.²⁰ And that reading of *Caronia* was adopted by a federal district court in the *Amarin Pharma v. FDA* case that was decided in August 2015.²¹

In *Amarin*, a pharmaceutical company wanted to promote off-label uses for one of its drugs, but it did not want to risk misbranding charges. Because its promotional speech was being chilled, the company asked the court to invalidate the off-label speech regulations. The *Amarin* court observed that under *Caronia*, prosecutions for off-label marketing entail prosecutions on the basis of speech and therefore have to meet the Supreme Court's heightened standard of review for restrictions on "commercial" speech. In applying the *Caronia* court's understanding of the heightened standard, the *Amarin* court concluded that the restrictions on off-label promotion were unconstitutional. But the *Amarin* opinion is incoherent. It essentially says that the government must prosecute for conduct not just for speech, and of course there is conduct involved in misbranding cases—the selling of drugs in interstate commerce.²²

19. To be sure, Mr. Caronia was charged with participating in a broad scheme to introduce misbranded drugs into interstate commerce. *Caronia*, 703 F.3d at 157–58. Nevertheless, his particular offense lay in his promotional speech. *Id.* at 159.

20. *Id.* at 164–69.

21. *Amarin Pharma, Inc. v. FDA*, 119 F. Supp. 3d 196, 224–28 (S.D.N.Y. 2015).

22. *Id.* at 228.

II. JUSTIFYING RESTRICTIONS ON OFF-LABEL MARKETING

One can mount three lines of defense against the First Amendment attack on the FDA's off-label marketing regulations.

A. Off-Label Marketing Restrictions Do Not Implicate the First Amendment

As the FDA observes, one can argue that there is no serious First Amendment issue. Companies are being charged with the sale of misbranded drugs, and the promotional advertising is relevant because it demonstrates a company's intent to introduce its drugs into interstate commerce for off-label uses.²³ It is common in criminal law to cite a defendant's speech as evidence of intent, and in such cases, consideration of the defendant's speech does not trigger the protection of the First Amendment.²⁴

Of course, there are serious First Amendment concerns when the government discriminates among speakers, and from one perspective that is what is happening with off-label marketing restrictions. Physicians are free to prescribe off label, and physicians, pharmacists, and anyone else can tout the off-label uses of a drug. Only the drug company's employees or contractors cannot promote off-label uses.²⁵ But the companies are not subject to prosecution simply for *discussing* off-label uses of their drugs; rather they are subject to prosecution for *selling* their drugs for off-label uses.

Consider the following example. Suppose a state permits marijuana use for medical purposes but not for recreational purposes. The government suspects that a grower is supplying marijuana to rogue marijuana dispensaries so those clinics can unlawfully sell marijuana for recreational purposes. Hence, an undercover government agent poses as the owner of a marijuana dispensary to check out the grower. If the grower discusses the opportunities for distribution of marijuana for recreational purposes during

23. Brief and Special Appendix for the United States at 51–54, *Caronia*, 703 F.3d 149 (2d Cir. 2012) (Nos. 09-5006-cr(L), 10-0750 (CON)), 2010 WL 6351497.

24. Robertson, *supra* note 10, at 549–50 (citing *Wisconsin v. Mitchell*, 508 U.S. 476, 489 (1993) and other authorities).

25. *Caronia*, 703 F.3d at 165.

conversations with the agent and encourages dispensing marijuana for recreational purposes, that could be used as evidence that the grower was conspiring to divert marijuana for illicit purposes.

Of course, recreational use of marijuana is unlawful in this hypothetical state while off-label use of prescription drugs is not unlawful in the United States. Perhaps that explains the difference between this hypothetical and the results in *Caronia* and *Amarin*. So suppose the state changes its ban on recreational marijuana to prohibit the *sale* of marijuana for recreational purposes but not the *use* of marijuana for recreational purposes. Rather than clogging its courts and prisons with users, the state wants to reserve its law enforcement resources for dealers. Under *Caronia* and *Amarin*, the marijuana grower could now invoke the First Amendment in a defense to the conspiracy charges. However, the applicability of the First Amendment to charges of illegal distribution should not hinge on whether use of a drug is illegal or not.

Scholars have presented other reasons to conclude that off-label marketing restrictions do not implicate the First Amendment. Christopher Robertson, for example, has argued that the FDA often should prevail in its regulation of off-label marketing at the first prong of the four-part *Central Hudson* test for commercial speech regulations. Under the first prong of *Central Hudson*, commercial speech does not receive protection under the First Amendment if the speech is false or misleading.²⁶ If promotional speech misleads physicians about the safety and effectiveness of a drug, patient welfare may be compromised. Accordingly, academic and judicial critics of the FDA's restrictions on off-label marketing routinely observe that the FDA is regulating speech that is truthful and not misleading.²⁷ But as Robertson points out, until a drug company or

26. *Caronia*, 703 F.3d at 165–66 (citing *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 566 (1980)). The speech also must be about lawful activity. If a company's commercial speech is not false or misleading, then the government can restrict it only if (a) the restrictions promote a substantial governmental interest, (b) the restrictions directly advance the governmental interest, and (c) the impact on the freedom of speech is not more extensive than necessary to serve the governmental interest. *Caronia*, 703 F.3d at 164 (citing *Cent. Hudson*, 447 U.S. at 566).

27. See *Caronia*, 703 F.3d at 160; Robertson, *supra* note 10, at 556–57. That is not the case with all prosecutions for off-label marketing. In a number of off-label cases, the

someone else conducts the studies necessary to prove the accuracy of the company's claims, courts are not in a position to deem promotional speech truthful and not misleading.²⁸ Rather than presuming the truth of the marketing claims, courts should expect drug companies to demonstrate the truth of their claims by obtaining approval for the new use from the FDA or by proving their claims before the court.²⁹

B. The Public Interest in Health Outweighs any First Amendment Concerns with Off-Label Marketing Regulations

Even if there is a serious First Amendment issue, the FDA can invoke important interests to justify its regulation of off-label promotional speech. That is, the FDA can defend its regulations on the ground that the public interest in good health is strong enough to overcome the individual interest in freedom of speech. In this view, the FDA regulations satisfy the heightened scrutiny that courts apply to restrictions on commercial speech under *Central Hudson*.³⁰

For example, under the final prong of the four-part test, courts consider whether there are alternate regulations that would serve the government's interests while having less of an impact on freedom of speech. Applying this standard, the district court in *Caronia* observed that it was unable to identify any alternate regulations that would sufficiently further the government's interest in having drug companies seek approval for new uses of their drugs.³¹

promotional speech was misleading. Lars Noah, *Permission to Speak Freely?*, 162 U. PA. L. REV. ONLINE 248, 248–49 (2014).

28. Robertson, *supra* note 10, at 558–60. See also Stephanie M. Greene, *FDA Prohibitions on Off-Label Marketing Do Not Violate Drug Manufacturers' First Amendment Rights*, 162 U. PA. L. REV. ONLINE 240, 242 (2014) (observing that the First Amendment defense to misbranding charges rests on “manufacturers’ unsubstantiated claims that the information they provide is in fact truthful and not misleading”).

29. Robertson, *supra* note 10, at 574. Of course, some promotional activities do not raise concerns about truthfulness, as when companies simply share copies of important peer-reviewed articles that report the results of a study of the drug's safety and effectiveness for an off-label use. The FDA permits drug companies to disseminate such articles without running afoul of the misbranding regulations. Revised Draft Guidance for Industry on Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices, 79 Fed. Reg. 11,793, 11,794–95 (Mar. 3, 2014).

30. For a description of the *Central Hudson* standard, see *supra* note 26.

31. *United States v. Caronia*, 576 F. Supp. 2d 385, 401 (E.D.N.Y. 2008). There is

C. Regulation of Drug Company Marketing Avoids Federalism Concerns

While defenses of FDA's regulations typically rest on the regulations' role in protecting the public's health, the regulations also can be justified on account of their role in ensuring proper respect for the principle of federalism and therefore in promoting proper respect for individual liberty.

According to the First Amendment critique of the FDA's off-label promotion regulations, if the FDA is concerned about off-label use of a prescription drug, the agency should regulate off-label use itself, thereby limiting off-label prescribing without infringing on freedom of speech.³² In *Caronia*, for example, the court observed that the government could impose "ceilings or caps on off-label prescriptions" or even, when off-label use is "exceptionally concerning, . . . prohibit the off-label use altogether."³³ The Supreme Court made a similar argument in the *Western States* case,³⁴ when it struck down restrictions on the advertising of drug "compounding" by pharmacists.³⁵ The *Western States* Court wrote that FDA could police inappropriate drug compounding by distinguishing between small-scale compounding for individual patients and large-scale

disagreement on this point. Even without incentives from the FDA, the reimbursement policies of insurers provide an incentive for pharmaceutical companies to seek approval for new uses since insurers often restrict reimbursement for off-label uses, Noah, *supra* note 27, at 249. Or the FDA might give companies other incentives to seek approval for new uses, including extended patent exclusivity, Lars Noah, *Truth or Consequences?: Commercial Free Speech vs. Public Health Promotion (at the FDA)*, 21 HEALTH MATRIX 31, 75 (2011).

32. That is, according to the First Amendment critique, off-label marketing restrictions fail the final prong of the *Central Hudson* test. See *supra* note 26.

33. *United States v. Caronia*, 703 F.3d 149, 168 (2d Cir. 2012). At times, the FDA does police off-label use of drugs, as in cases in which there are serious side effects from the uses. *Klasmeier & Redish, supra* note 5, at 336–37. But exceptional interventions do not require the same degree of federal oversight as would routine regulation of off-label uses.

34. *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 372 (2002).

35. *Id.* at 360. For most patients, pharmacists dispense pills that have been manufactured by a pharmaceutical company. But for some patients, the pharmacist actually creates a medication that is tailored to the needs of that patient. *Id.* at 360–61. As the *Western States* Court wrote, "[c]ompounding is typically used to prepare medications that are not commercially available, such as medication for a patient who is allergic to an ingredient in a mass-produced product." *Id.* at 361. Compounding also can be used to provide drugs in forms that are more palatable for children (e.g., as a pleasantly-flavored syrup rather than a medicinal-tasting tablet). See *id.* at 377.

compounding for bulk sales, rather than by distinguishing between advertised and unadvertised compounding.³⁶

The distinction between regulating speech and regulating conduct generally makes sense under First Amendment doctrine, but in the case of off-label drug prescribing, regulations of conduct raise serious federalism concerns. For the FDA to regulate off-label use directly, it would have to police the day-to-day interactions between patient and physician. It would have to substitute its judgment about the propriety of a prescription in place of the physician's medical judgment. It is one thing for the FDA to decide whether a drug is sufficiently safe and effective to allow its sale by pharmaceutical companies. It is quite another matter for the FDA to decide whether a drug should be prescribed by physicians to particular patients. Historically, governmental regulation of individual prescription decisions has been through state rather than federal action. The fifty states have regulated prescription decisions through their rules for professional liability and professional discipline. If there is reason to believe a physician is inappropriately prescribing a drug, then the licensing board can act, and patients can sue for malpractice. In short, the argument against regulation of off-label marketing is an argument in favor of the FDA setting its own standards for an important aspect of the practice of medicine, and that would entail a major substitution of federal authority for a government authority that traditionally is exercised by states.³⁷

While it is common to view federalism principles as protecting state government authority from encroachment by the federal government, the federalism doctrine ultimately serves as a safeguard for individual liberty. As the Supreme Court has observed, “[s]tate sovereignty is not just an end in itself: ‘Rather, federalism secures to citizens the liberties that derive from the diffusion of sovereign power.’”³⁸ The state government is generally more accountable than

36. *Id.* at 371–72.

37. A similar federalism-based argument could have been made in *Western States*. By regulating advertising of compounding rather than compounding itself, the federal government deferred to state regulation of pharmacy practices.

38. *New York v. United States*, 505 U.S. 144, 181 (1992) (citing *Coleman v. Thompson*, 501 U.S. 722, 759 (1991)) (Blackmun, J., dissenting)).

is the federal government to a state's citizens;³⁹ moreover, state regulation allows for variation in approaches, and Americans can settle in states whose regulatory regimes are most appealing to them.⁴⁰ Hence, when the *Caronia* and *Amarin* courts invoked First Amendment principles to protect individual liberty, they were sacrificing one liberty-protecting constitutional principle—the principle of federalism—for another liberty-protecting constitutional principle—the freedom to speak. As a result, the courts did nothing to advance the interest in liberty and contain governmental power.

To put it another way, critics of FDA off-label marketing regulations want the FDA to distinguish between appropriate and inappropriate uses of a drug rather than between the use of a drug and the marketing of a drug. Focusing on whether an off-label use is appropriate avoids potential First Amendment problems, but it creates federalism problems. The FDA's approach to off-label use of prescription drugs allows it to draw a line between regulating a matter of national concern—interstate commerce in prescription drugs—and not regulating a matter of local concern—the practice of medicine. The desire by the federal government to respect principles of federalism should count as sufficient reason for regulating promotional speech.⁴¹

I do not mean to suggest that regulation of off-label prescribing would exceed the federal government's power to regulate interstate commerce. Though prescribing regulations would be unconstitutional under Justice Clarence Thomas' view of the Commerce Clause,⁴² such regulation would fit within the Supreme Court's current limits for the commerce power. Nevertheless, as the Court observed in *Lopez*, federal government intrusion into matters of local concern, such as K–12 education and family law, raise serious constitutional concerns.⁴³ The same concerns are raised by intrusion into the

39. *Nat'l Fed'n of Indep. Bus. v. Sebelius*, 132 S. Ct. 2566, 2578 (2012).

40. GEOFFREY R. STONE ET AL., *CONSTITUTIONAL LAW* 161–62 (7th ed. 2013).

41. Under the *Central Hudson* standard for commercial speech, the desire to preserve principles of federalism would count as a substantial interest under the second prong of the standard.

42. *United States v. Lopez*, 514 U.S. 549, 584–92 (1995) (Thomas, J., dissenting).

43. *Id.* at 564 (majority opinion). Because of concerns about federal intrusion into state authority with exercises of the commerce power, most federal regulation of medical practice

traditional local concern of medical practice. Courts should encourage federal government respect for state government authority by giving substantial weight to decisions by the federal government not to exercise its powers to their fullest extent.

Even if the FDA should not regulate off-label prescribing, what about other alternatives to the regulation of off-label marketing? Recall that under the final prong of the *Central Hudson* test, regulations of off-label marketing are not permitted if there are alternate regulations that would achieve the FDA's goals with a smaller impact on the freedom of speech.⁴⁴ Thus, for example, the *Caronia* court discussed the option of counter-speech by the government as an alternate regulation.⁴⁵ Instead of restricting pharmaceutical company speech, the FDA could respond to promotional speech with its own speech.

It is difficult to see how counter-speech would be sufficiently effective at serving the government's interests. Pharmaceutical companies spend billions of dollars annually to promote their products to physicians. And much of that money is used to employ tens of thousands of sales representatives who meet with physicians and pitch the companies' drugs.⁴⁶ To respond effectively to off-label marketing with counter-speech, the FDA would have to establish its own army of representatives to meet with physicians on an individual basis, and it would have to know which physicians were receiving which off-label pitches from pharmaceutical salespersons. That is not a realistic option.⁴⁷

occurs through the spending power, as when Congress conditions participation in Medicare or Medicaid on adherence to practice regulations.

44. See *supra* note 26.

45. *United States v. Caronia*, 703 F.3d 149, 168 (2d Cir. 2012).

46. Prescription Project, *Persuading the Prescribers: Pharmaceutical Industry Marketing and Its Influence on Physicians and Patients*, PEW CHARITABLE TRUSTS (Nov. 11, 2013), www.pewtrusts.org/en/research-and-analysis/fact-sheets/2013/11/11/persuading-the-prescribers-pharmaceutical-industry-marketing-and-its-influence-on-physicians-and-patients.

47. For further discussion of the inadequacies of counter-speech, see Kesselheim, *supra* note 8, at 250–51.

CONCLUSION

When the government restricts the freedom to speak, there is good reason to worry that individual liberty is being compromised. Critics of off-label marketing restrictions are right to ask whether First Amendment rights are being violated.

Upon careful examination, however, First Amendment concerns should not block regulation of off-label marketing. A company's off-label promotional speech provides probative evidence of illicit conduct—the distribution of misbranded drugs—and therefore restrictions of off-label promotion should not trigger First Amendment protection. In addition, the First Amendment does not shield promotional speech that is misleading or untruthful. Accordingly, pharmaceutical companies should not be able to invoke First Amendment protections unless they provide substantiation for the claims they make about off-label uses of their drugs. Even if First Amendment rights apply, limits on the marketing of off-label uses should survive. The FDA relies on its regulation of off-label promotion as an alternate to the direct regulation of off-label prescribing, and this choice actually protects individual liberty by restraining the federal government's intrusion into the regulatory space of the states. Courts should reject the reasoning of the *Caronia* court and preserve the authority of the FDA to regulate off-label marketing by drug companies.