

Off-Label Marketing and the First Amendment

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On December 3, 2012, a three-judge panel of a U.S. appeals court took a controversial leap toward what some fear will be license by the courts to invalidate a host of state and federal regulations, including some applicable to health care. In recent years, the Supreme Court has broadened the reach of the First Amendment, defining “protected speech” in such a way as to curtail or eliminate certain familiar governmental restraints. (See table for an overview of cases related to commercial speech and the pharmaceutical industry.) At issue in the December 3 opinion — which is doubtless headed for further appeal — were the Food and Drug Administration (FDA) regulations applicable to marketing of prescription pharmaceuticals for off-label uses. Overturning the conviction of a sales representative who was found to have engaged in off-label promotion of a prescription drug, a three-judge panel of the U.S. Court of Appeals for the Second Circuit (New York) held in *United States v. Caronia* that “the government cannot prosecute pharmaceutical manufacturers and their representatives under the [Food, Drug, and Cosmetic Act] for speech promoting the lawful, off-label use of an FDA-approved drug.”¹

In 2011, in *Sorrell v. IMS Health*,² the precursor to *Caronia*, the U.S. Supreme Court held that a pharmaceutical marketing tool known as data mining — purchasing information about prescribers from pharmacies and others and selling it to pharmaceutical companies — may be protected by the

First Amendment, and the Court invalidated a Vermont law that prohibited the practice. Just a year earlier, in a similar expansion of First Amendment protections, the Court had overturned portions of the McCain–Feingold Act, which limited the spending of tax-exempt political organizations, holding that campaign contributions may constitute commercial speech that is entitled to the protection of the First Amendment.³ Now, the Second Circuit has seized the first appellate opportunity since *Sorrell* to interpret that Supreme Court precedent in the context of FDA restrictions concerning off-label drug marketing. Alfred Caronia, a pharmaceutical detailer, defended his off-label marketing with the argument that the FDA regulations prohibiting it infringed his First Amendment right of free speech and were therefore void.

The FDA is vested with the responsibility of overseeing the safety of pharmaceutical production and the veracity of marketing. Its rigorous approval process requires that each new product be tested for safety and efficacy for each intended use. Although FDA regulations warn that it is considered “misbranding” for marketers to “recommend or suggest” that a drug is appropriate for an indication for which it has not specifically been approved, the FDA’s authority does not extend to the practice of medicine, and thus it cannot prohibit physicians from prescribing approved drugs for nonapproved uses.

The Vermont law at issue in *Sorrell* permitted mining of physi-

cians’ prescribing data from patient information for some purposes (e.g., research), but not for others (primarily marketing), in order to advance the state’s goal of limiting the promotion of expensive, brand-name products. The Supreme Court held that a law that constrains speech on the basis of its content and its speaker must be reviewed for First Amendment purposes, applying a standard of “heightened” constitutional scrutiny. Although it acknowledged the importance of Vermont’s asserted interests in medical privacy and the reduction of health care costs, the Court nevertheless concluded that Vermont’s data-mining prohibition unduly restricted free speech and was therefore unconstitutional.

At the heart of *Sorrell* was the question of whether governments are permitted to enact regulations, even those protecting the health of the public, that single out a particular industry (e.g., the pharmaceutical industry) and allow some messages (e.g., promoting brand-name drugs for off-label uses) but not others. As noted in the dissent, traditional regulatory programs do, in fact, target particular industries, and when they are narrowly tailored to advance significant state objectives, they have generally been upheld. The key to passing constitutional scrutiny is whether the law at issue discriminates on the basis of the content of the message.

Disposing first of Vermont’s argument that data mining involves conduct rather than speech, *Sorrell* held that the creation and

Recent Legal Decisions Related to Commercial Speech and the Pharmaceutical Industry.

Case	Highest Court	Date	Law	Decision
<i>IMS v. Ayotte</i>	First Circuit Court of Appeals	November 2008	New Hampshire Prescription Information Law, the first law in the nation to ban the use of a physician's prescribing data for pharmaceutical marketing	First Circuit Court of Appeals in Boston overturns the District Court and rules that the New Hampshire law permissibly restricts the conduct of data collection and does not impermissibly restrict the speech of pharmaceutical companies.
<i>IMS v. Rowe</i>	First Circuit Court of Appeals	August 2010	Confidentiality of Prescription Drug Information Act, restricting drug makers' access to prescribing data	First Circuit overturns U.S. District Court ruling that Maine state law unconstitutionally restricts freedom of commercial speech.
<i>Sorrell v. IMS</i>	U.S. Supreme Courts	June 2011	Vermont Pharmaceutical Data Mining Law	U.S. Supreme Court strikes down Vermont law saying the statute violates the First Amendment.
<i>United States v. Caronia</i>	Second Circuit Court of Appeals	December 2012	Provision of Food, Drug, and Cosmetic Act banning off-label marketing	Second Circuit throws out conviction for off-label promotion as violation of First Amendment right to free speech.

distribution of information is in fact speech: "Facts, after all, are the beginning point for much of the speech that is most essential to advance human knowledge and to conduct human affairs." Applying First Amendment principles, the Court found the Vermont law to be discriminatory in that it suppressed a particularly effective, albeit distasteful, message. The majority concluded, "If pharmaceutical marketing affects treatment decisions, it does so because doctors find it persuasive," and "the fear that speech might persuade provides no lawful basis for quieting it."

Waiting in the First Amendment wings, *Caronia* involved a sales representative of Orphan Medical, a subsidiary of Jazz Pharmaceuticals, who was assigned to promote the prescription drug Xyrem (sodium oxybate), a central nervous system depressant approved for the treatment of cataplexy and narcolepsy (including daytime sleepiness) in adults. Xyrem is a Schedule III controlled substance known to be abused

by young adults. It is used off-label to treat children for cataplexy and narcolepsy and to treat adults for a variety of conditions, including fibromyalgia, schizophrenia, chronic fatigue syndrome, and severe cluster headaches. Caronia and a physician from Orphan gave talks and met individually with prescribers to promote Xyrem, allegedly for off-label uses. Suspecting that this illegal marketing was taking place, the Department of Justice conducted a sting operation, secretly recording one such meeting. Caronia and the physician were both indicted for off-label drug promotion.

Challenging the constitutionality of the misbranding charges, Caronia argued that the government cannot restrict truthful, non-misleading commercial speech promoting the use of a pharmaceutical product, even off-label. The trial court — a federal district court in New York — found against Caronia, holding that "constraining the marketing options of manufacturers is one of

the few mechanisms available to the FDA to ensure that manufacturers will not seek approval only for certain limited uses of drugs, then promote that same drug for off-label uses, effectively circumventing the FDA's new drug requirements."⁴ Heeding a 2008 cautionary note from the Seventh Circuit that a "court should hesitate before extending . . . [a] historical reading of the Constitution in a way that injures the very audience that is supposed to benefit from free speech,"⁵ and concluding that it could not identify a less restrictive manner in which to prohibit pharmaceutical companies from circumventing the FDA approval process, the trial court in *Caronia* upheld the constitutionality of the FDA regulations, concluding that "any right Caronia had as Xyrem's sales representative to express as commercial speech the truthful promotion of Xyrem's off-label uses is not unconstitutionally restricted by the misbranding provisions"⁴ of the FDA.

In overturning Caronia's con-

viction, the three-judge panel of the Second Circuit agreed that the FDA regulations were overly broad, specifically noting that nothing Caronia did constituted conspiracy to put a false or misleading or deficient label on a drug product. The court appeared particularly persuaded by the argument that the FDA regulations allow unfettered prescribing of approved drugs for off-label uses but then, through the off-label restrictions, refuse to allow the free flow of information that would result in a full vetting of the uses, limitations, and side effects of the drug. The Second Circuit held that such restrictions violate the principles of the First Amendment.

Caronia and *Sorrell*, as well as other recent Supreme Court cases striking down governmental regulations in favor of free expression, raise significant concerns about the ability of the state and federal governments to impose a variety of regulatory programs targeting specific conduct or a particular industry. Indeed, the *Sorrell* dissent had made clear that the Court was casting a wide net — potentially broad enough to engulf the FDA's off-label regulations designed to combat false and misleading speech. The question now is whether a host of other state and federal regulations can withstand such First Amendment scrutiny.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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1. U.S. v. Caronia. 09-5006-CR (http://www.ca2.uscourts.gov/decisions/isysquery/1aec774e-1fe9-4631-bdf3-69a6d0c06b93/11/doc/09-5006_complete_opn.pdf#xml=http://www.ca2.uscourts.gov/decisions/isysquery/1aec774e-1fe9-4631-bdf3-69a6d0c06b93/11/hilite/).
2. 131 S. Ct. 2653, 2668 (2011).
3. Citizens United v. Federal Election Commission, 558 U.S. 50, 130 S. Ct. 876 (2010).
4. U.S. v. Caronia, 576 F. Supp. 2d 385, 401 (E.D.N.Y.2008).
5. U.S. v. Caputo, 517 F.3d 935, 939 (7th Cir.2008).

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