

2011

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Kristie LaSalle, *A Prescription for Change: Citizens United's Implications for Regulation of Off-Label Promotion of Prescription Pharmaceuticals*, 19 J. L. & Pol'y (2011).

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A PRESCRIPTION FOR CHANGE: CITIZENS UNITED'S IMPLICATIONS FOR REGULATION OF OFF-LABEL PROMOTION OF PRESCRIPTION PHARMACEUTICALS

*Kristie LaSalle**

I. INTRODUCTION

Al Caronia, a pharmaceutical sales representative for Orphan Pharmaceuticals, a subsidiary of Jazz Pharmaceuticals, walked into a physician's office in Great Neck, New York on November 2, 2005.¹ He had received several phone calls from the physician asking about Xyrem,² Orphan's medication for the treatment of

* J.D. Candidate, Brooklyn Law School, 2012; B.A. Biology, Swarthmore College, 2006. I owe an immeasurable debt of gratitude to Professor Aliza Kaplan, not only for teaching me to write, but for her tireless support and encouragement, and countless hours spent assisting in the writing and editing process. This Note could not have been possible without her love and support. I would like to thank Professors William Araiza and Joel Gora; Paul V. Avelar, James Beck, and Adam Michaels, Esqs.; and Robert Sobelman, J.D. Candidate, Brooklyn Law School, 2012; for their support, guidance, and suggestions during the writing process. I would also like to thank the entire editorial staff of the Journal of Law and Policy for their editorial assistance. Finally, thank you to my family, Richard, Cathy, Kimberlee, and Cadie for their support in all of my endeavors.

¹ Brief for Petitioner at 4, *United States v. Caronia*, No. 09 Cr. 5006 (2d Cir. filed Apr. 15, 2010) [hereinafter *Caronia Brief*]; Appendix to *Caronia Brief* at A-32 (transcript of conversation, indicating physicians' office address).

² *Id.* at 3. This physician was an internal medicine specialist who, unbeknownst to Mr. Caronia, had never prescribed a single narcoleptic. *Id.* Prior to receiving phone calls from the physician, Mr. Caronia had never met him; however, after receiving repeated phone calls, Mr. Caronia decided to add the physician to the list of doctors whom he visited, and met with him for the first time on October 26, 2005. *Id.* At the October 26 meeting, the physician asked

cataplexy,³ a muscle disorder associated with narcolepsy,⁴ so Mr. Caronia brought Dr. Peter Gleason with him to discuss his experience prescribing the medicine.⁵ Mr. Caronia sat silently while Dr. Gleason spoke with the physician, answering questions about Xyrem's different uses, including the treatment of Excessive Daytime Sleepiness ("EDS"), a new use then under review by the Food and Drug Administration ("FDA").⁶ So promising was that treatment, in fact, that the FDA approved Xyrem for treatment of EDS on November 18, 2005,⁷ just sixteen days after Mr. Caronia and Dr. Gleason visited the physician's office. A year and a half later, however, on July 25, 2007, a federal grand jury indicted Mr. Caronia and Dr. Gleason for illegally promoting a prescription pharmaceutical.⁸ The physician, it turned out, was a confidential informant for the FDA, and the Federal Bureau of Investigation ("FBI") had recorded his meetings with Mr. Caronia and Dr. Gleason.⁹ Prior to trial, Dr. Gleason pleaded guilty to a reduced charge, becoming the first physician convicted of misbranding a drug.¹⁰ Mr. Caronia was found guilty of criminally misbranding a

Mr. Caronia about several unapproved, or off-label, uses of Xyrem, and asked to meet Dr. Gleason, a prominent physician in the field with experience prescribing Xyrem. *Id.* at 3–4.

³ XYREM PRODUCT LABEL at 6 (July 17, 2002), available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2002/21196lbl.pdf. Xyrem is a sleep-inducing depressant. *Id.*

⁴ Nat'l Inst. of Neurological Disorders and Stroke, *Narcolepsy Fact Sheet*, NAT'L INSTS. HEALTH (last updated May 14, 2010), http://www.ninds.nih.gov/disorders/narcolepsy/detail_narcolepsy.htm. Cataplexy is a debilitating symptom of narcolepsy, triggered by strong emotions like anger or fear. It manifests as a loss in muscle control, with the most severe cases resulting in physical collapse and the inability to move, speak, or open one's eyes. *Id.*

⁵ United States v. Caronia, 576 F. Supp. 2d 385, 389–90 (E.D.N.Y. 2008).

⁶ Caronia Brief, *supra* note 1, at 4; Appendix to Caronia Brief, *supra* note 1, at A-41 (transcript of conversation, discussing the use of Xyrem for EDS).

⁷ Letter from Russell Katz, Dir., Div. of Neurology Prods., Ctr. for Drug Eval., FDA, to Dr. Reardan, Orphan Med., Inc. (Nov. 18, 2005).

⁸ See Indictment, United States v. Caronia, 576 F. Supp. 2d 385 (E.D.N.Y. 2008) (No. 06 Cr. 229).

⁹ Appendix to Caronia Brief, *supra* note 1, at A-32.

¹⁰ *Judge Strikes Down First Amendment Arguments In Pharmaceutical Sales Representative Federal Trial*, FDA ADVER. & PROMOTION MANUAL &

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prescription pharmaceutical for promoting Xyrem for EDS,¹¹ even though the information related to the efficacy of Xyrem in treating EDS was accurate and non-misleading, as evidenced by the FDA's approval of such a use a mere two weeks later. Why?

The FDA forbids drug manufacturers from marketing their products for any use not expressly approved by the FDA.¹² Promotion of an unapproved use is deemed off-label promotion,¹³ and may result in criminal and civil sanctions.¹⁴ The regulatory

NEWSL. 9 (FDA, Washington, D.C. Nov. 2008).

¹¹ Appendix to Caronia Brief, *supra* note 1, at A-85 to A-86 (verdict sheet).

¹² See Food, Drug, & Cosmetic Act, 21 U.S.C.A. § 331 (West 2010).

¹³ Wash. Legal Found. v. Kessler, 880 F. Supp. 26, 28 n.1 (D.D.C. 1995) (Off-label use "refers to the use of a drug or device in a manner not approved by the FDA and not set forth in the product's labeling materials.").

¹⁴ 21 U.S.C.A. § 333. Many United States Attorneys' Offices (USAOs), especially the District of Massachusetts, the Eastern District of Pennsylvania, and the Northern District of California, aggressively prosecute misbranding infractions. See, e.g., Press Release, USAO, N. Dist. Cal., W. Scott Harkonen, Former Biotech CEO, Convicted of Wire Fraud (Sept. 29, 2009), available at http://www.justice.gov/usao/can/press/2009/2009_09_29_harkonen.convicted.press.html (announcing conviction of pharmaceutical CEO for promoting Actimmune for an off-label use); Press Release, USAO, Dist. Mass., Drug Maker Forest Pleads Guilty; Will Pay More Than \$313 Million to Resolve Criminal Charges and False Claims Act Allegations (Sept. 15, 2010), available at <http://www.justice.gov/usao/ma/Press%20Office%20-%20Press%20Release%20Files/Sept2010/SettlementPressRelease.html>; Press Release, USAO, Dist. Mass., Pharmacia & Upjohn Company Inc. Pleads Guilty to Fraudulent Marketing of Bextra (Sept. 15, 2009), available at <http://www.justice.gov/usao/ma/Press%20Office%20-%20Press%20Release%20Files/Sept2009/PharmaciaPlea.html>; Press Release, U.S. Dep't Health and Human Servs., Justice Department Announces Largest Health Care Fraud Settlement in Its History (Sept. 2, 2009), available at <http://www.hhs.gov/news/press/2009pres/09/20090902a.html> (announcing \$2.3 billion settlement in the District of Massachusetts); Press Release, USAO, E. Dist. of Pa., Pharmaceutical Company Eli Lilly to Pay Record \$1.415 Billion for Off-Label Drug Marketing (Jan. 15, 2009), available at <http://www.justice.gov/usao/pae/News/Pr/2009/jan/lilly.release.pdf>; Press Release, Dep't of Justice, Pharmaceutical Giant AstraZeneca to Pay \$520 Million for Off-label Drug Marketing (Apr. 27, 2010), available at <http://www.justice.gov/opa/pr/2010/April/10-civ-487.html> (announcing a plea deal in the Eastern District of Pennsylvania).

scheme surrounding off-label promotion¹⁵ is murky at best, and leaves manufacturers little absolute guidance.¹⁶ Policy is delineated largely by the FDA's own interpretation of its regulatory power, disseminated piecemeal in guidance documents, and often driven by the FDA's response to private litigation or other emerging issues.¹⁷

Until recently, a similar regulatory scheme existed in a seemingly unrelated field of free speech jurisprudence: corporate political speech.¹⁸ Few recent Supreme Court decisions have garnered as much criticism as the 2010 decision in *Citizens United v. FEC*,¹⁹ in which the Supreme Court held that the Federal

¹⁵ See 21 U.S.C.A. §§ 301–99; see generally *infra* Part II.B.

¹⁶ See generally, e.g., FOOD AND DRUG ADMIN., GOOD REPRINT PRACTICES FOR THE DISTRIBUTION OF MEDICAL JOURNAL ARTICLES AND MEDICAL OR SCIENTIFIC REFERENCE PUBLICATIONS ON UNAPPROVED NEW USES OF APPROVED DRUGS AND APPROVED OR CLEARED MEDICAL DEVICES, (Jan. 2009) [hereinafter GOOD REPRINT PRACTICES] available at <http://www.fda.gov/oc/op/goodreprint.html>.

¹⁷ For example, in one challenge to the FDA's prohibition of off-label promotion, the FDA stipulated that no previous guidance document "independently authorizes the FDA to prohibit or sanction speech," rendering moot an injunction against prohibiting certain forms of off-label promotion imposed at the trial court level. *Wash. Legal Found. v. Henney (WLF III)*, 202 F.3d 331, 335 (D.C. Cir. 2000). The FDA then promptly issued a guidance document, interpreting the Circuit Court's ruling as a holding that the "FDA, consistent with its longstanding interpretation of the laws it administers, may proceed, in the context of case-by-case enforcement, to determine from a manufacturer's written materials and activities how it intends that its products be used." Notice; Decision in *Washington Legal Foundation v. Henney*, 65 Fed. Reg. 14,286 (Mar. 16, 2000) [hereinafter *WLF III* Decision Notice].

¹⁸ See generally *Citizens United v. F.E.C.*, 130 S. Ct. 876 (2010).

¹⁹ *Id.*; see, e.g., Ronald Dworkin, *The "Devastating" Decision*, N.Y. REV. BOOKS, Feb. 25, 2010, at 39 (reporting the *Citizens United* decision arose from the Court's political preference for the Republican Party and/or its general favoritism of corporate interests); Molly J. Walker Wilson, *Too Much of a Good Thing: Campaign Speech After Citizens United*, 31 CARDOZO L. REV. 2365, 2368–69 (2010); Adam Liptak, *Justices, 5-4 Reject Corporate Spending Limit*, N.Y. TIMES, Jan. 21, 2010, at A1. Perhaps the most well-known criticism of the holding came from President Obama. Barack Obama, Remarks by the President in the State of the Union Address (Jan. 27, 2010) ("[L]ast week, the Supreme Court reversed a century of law that I believe will open the floodgates for

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Elections Commission's ("FEC") regulation of corporate political expenditures was unconstitutional.²⁰ Much of the criticism focused on the case's implications for campaign finance;²¹ however, the Court's language and reasoning²² may have dramatic implications for other areas of speech. In particular, *Citizens United* may signal a dramatic increase in the rights of those engaged in heavily-regulated—and, to this point, heavily suppressed—commercial speech.²³ One area of commercial speech jurisprudence that may change after *Citizens United* is the off-label promotion of pharmaceutical products.

The *Citizens United* holding portrays an inherent mistrust of the use of convoluted regulatory schemes to abridge speech. The Court held that a muddled regulatory scheme essentially functions as a prior restraint: it leaves a potential speaker with the constitutionally unpalatable choice between remaining silent or asking the government whether its speech is lawful.²⁴ Justice Kennedy's declaration that prohibition of corporate independent expenditures constituted an "unprecedented governmental intervention into the realm of speech,"²⁵ however, is misplaced: a similar intrusion on speech rights exists in pharmaceutical marketing regulation.²⁶ The FDA's prohibition of off-label promotion applies regardless of whether the marketing message the manufacturer wishes to disseminate is truthful and non-

special interests—including foreign companies—to spend without limit in our elections I don't think American elections should be bankrolled by America's most powerful interests, or worse, by foreign entities.").

²⁰ *Citizens United*, 130 S. Ct. at 913.

²¹ See generally Wilson, *supra* note 19. This Note takes no normative position on the wisdom or failings of *Citizens United* as applied to political speech.

²² See *Citizens United*, 130 S. Ct. at 896 (finding that muddled regulatory schemes function as a prior restraint on speech).

²³ See *infra* Part III. See also, generally, Tamara R. Piety, *Citizens United and the Threat to the Regulatory State*, 109 MICH. L. REV. FIRST IMPRESSIONS 16 (2010).

²⁴ *Citizens United*, 130 S. Ct. at 896.

²⁵ *Id.*

²⁶ See generally Food, Drug & Cosmetic Act, 21 U.S.C.A. §§ 301–99 (West 2010); GOOD REPRINT PRACTICES, *supra* note 16.

misleading.²⁷ The FDA's transgressions upon the manufacturers' speech rights bear many of the marks condemned in *Citizens United*: the regulation constitutes "an outright ban [on speech], backed by criminal sanctions";²⁸ the FDA regulates speech by "carving out a limited exemption through an amorphous regulatory interpretation";²⁹ and in doing so, the FDA paternalistically "select[s] what . . . speech is safe for public consumption by applying an ambiguous test."³⁰ Thus, under *Citizens United*, the FDA's prohibition of off-label promotion constitutes an unconstitutional abridgement of commercial speech.

Fortunately, the similarities between the infirmities of the FEC's regulation of independent corporate political expenditures at issue in *Citizens United* and those of the FDA's regulation of off-label promotion suggest that the solutions posed in *Citizens United* to enable continuing regulation while respecting corporations' political speech rights³¹ will also cure the constitutional failings of the FDA's off-label regulation. When properly construed, the government's interest in promoting the public health and safety may be adequately addressed by requiring the speaker—that is, the pharmaceutical manufacturer—to disclose the off-label nature of its promotions.³²

At the outset, clarification is necessary as to the limited form of off-label promotion for which this Note advocates greater First Amendment protection. That limited category of speech is (1) truthful, accurate, and not misleading;³³ (2) directed only to other

²⁷ See 21 U.S.C.A. §§ 351–52. *Contra* Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n N.Y., 447 U.S. 557, 566 (1980) (finding that, for commercial speech to warrant First Amendment protection, "it at least must . . . not be misleading"); 44 Liquormart v. Rhode Island, 517 U.S. 484, 510 (1996) ("[I]n keeping with our prior holdings, we conclude that a state legislature does not have the broad discretion to suppress truthful, nonmisleading information for paternalistic purposes. . . .").

²⁸ *Citizens United*, 130 S. Ct. at 897. See also 21 U.S.C.A. § 333 (describing criminal and civil sanctions that attend misbranding).

²⁹ See *Citizens United*, 130 S. Ct. at 889.

³⁰ See *id.* at 896.

³¹ See *id.* at 915.

³² See *id.*

³³ Fraudulent or inherently misleading commercial speech receives no First

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prescribing healthcare professionals;³⁴ and (3) relates to off-label uses of FDA-approved drugs only. Such speech would benefit the public at large, were it to be permitted.³⁵ Physicians may prescribe a medication for any use, including off-label uses.³⁶ Indeed, the FDA itself recognizes that off-label prescribing may be safe, and sometimes the standard of care for a particular patient or disease.³⁷ Providing the proper constitutional protection for truthful, non-misleading off-label promotion would facilitate the dissemination of medical information to physicians. As explained below, public health will be enhanced by dissemination of such information, resulting in better-informed prescribing decisions by physicians.³⁸

This Note addresses the First Amendment concerns implicated by the FDA's policies prohibiting off-label promotion of prescription medications, and presents a potential solution. Part II of this Note surveys the current state of the constitutional, statutory, and regulatory frameworks, as well as the litigation landscape, surrounding off-label promotion. Part III demonstrates that *Citizens United's* rationale extends beyond political speech to heavily-regulated commercial speech. Specifically, the Court's concern that the FEC's complex and "amorphous regulatory interpretation"³⁹ constitutes a restriction so inscrutable that it functions as a prior restraint finds a ready parallel in the FDA's regulation of off-label promotion.

Finally, in applying the Court's commercial speech analysis

Amendment protection. *See infra* Part II.A; *Kasky v. Nike, Inc.*, 45 P.3d 243, 306 (Cal. 2002) (noting that, although some false political speech receives First Amendment protection, the protection does not extend to false commercial speech); *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n N.Y.*, 447 U.S. 557, 566 (1980); *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council*, 425 U.S. 748, 771 (1976) ("Untruthful speech, commercial or otherwise, has never been protected for its own sake.").

³⁴ This Note does not discuss the constitutional implications of the FDA's regulation of Direct to Consumer (DTC) marketing.

³⁵ *See infra* Part IV.B.

³⁶ *Use of Approved Drugs for Unlabeled Indications*, 12 FDA DRUG BULL. 4 (FDA, Washington, D.C., Apr. 1982).

³⁷ GOOD REPRINT PRACTICES, *supra* note 16, § III.

³⁸ *See infra* Part IV.B.

³⁹ *Citizens United v. F.E.C.*, 130 S. Ct. 876, 889 (2010).

and the principles informing *Citizens United*, this Note concludes in Part IV that the FDA's current policies regarding off-label promotion are unconstitutional under the First Amendment. A commercial speech analysis, the test for which was set forth in *Central Hudson Gas and Electric Corporation v. Public Service Commission of New York*,⁴⁰ reveals that the constitutional failing is twofold. First, the FDA, and courts who have previously considered the constitutionality of the FDA's prohibition on speech, have misconstrued the purported government interest:⁴¹ rather, when properly construed, the interest is not advanced by—and in fact may be hindered by—the prohibition of off-label promotion. Second, the current policy is more restrictive than necessary to serve that interest. Using *United States v. Caronia*⁴² as an example, this Note advocates the adoption of a disclosure regime, as approved of in *Citizens United*, which would better serve public health while being less restrictive of speech.

II. COMMERCIAL SPEECH CHILLED: THE STATUTORY, REGULATORY, AND LEGAL LANDSCAPE OF OFF-LABEL PROMOTION

Regardless of whether it is classified as pure, scientific, speech or commercial speech,⁴³ off-label promotion of prescription pharmaceutical products is entitled to some First Amendment

⁴⁰ *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n N.Y.*, 447 U.S. 557, 566 (1980); *see infra* Part II.A.

⁴¹ *See United States v. Caputo*, 288 F. Supp. 2d 912, 921 (N.D. Ill. 2003) (announcing as a substantial government interest “the government’s interest in subjecting off-label uses to the FDA’s evaluation process as well as the government’s interest in preserving the integrity of the [Food Drug and Cosmetic Act’s] new drug approval process”); *see also, generally, infra* Part IV.A.

⁴² *United States v. Caronia*, 576 F. Supp. 2d 385 (E.D.N.Y. 2008).

⁴³ Although beyond the scope of this Note, there is good reason to question whether off-label promotion is truly commercial speech or whether it is in fact scientific, and therefore pure, speech entitled to the highest constitutional protection. *See generally, e.g.*, Glenn C. Smith, *Avoiding Awkward Alchemy—In the Off Label Drug Context and Beyond: Fully-Protected Independent Research Should Not Transmogrify into Mere Commercial Speech Just Because Product Manufacturers Distribute It*, 34 WAKE FORREST L. REV. 963 (1999).

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protection.⁴⁴ Yet under the current regulatory regime created by the FDA, off-label promotion is all but prohibited.⁴⁵ Challenges to the constitutionality of this absolute prohibition have thus far done little to vindicate manufacturers' First Amendment rights.⁴⁶

A. The Commercial Speech Doctrine

Despite the constitutional mandate that “Congress shall make no law . . . abridging the freedom of speech,”⁴⁷ commercial speech, or speech which “does no more than propose a commercial transaction,” has historically received diminished protection under the First Amendment.⁴⁸ Until the 1970s, commercial speech was entitled to no constitutional protection whatsoever.⁴⁹ In 1976, the Supreme Court afforded limited constitutional protection to commercial speech.⁵⁰ In *Virginia Board of Pharmacy v. Virginia Citizens Consumer Council*, the Court struck down a state ban on

⁴⁴ See *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council*, 425 U.S. 748, 761 (1976); see generally *Central Hudson*, 447 U.S. 557 (extending, for the first time, qualified First Amendment protection to commercial speech); see generally *infra* Part II.A.

⁴⁵ See generally Food, Drug & Cosmetic Act, 21 U.S.C.A. §§ 301–99 (West 2010); GOOD REPRINT PRACTICES, *supra* note 16; see generally *infra* Parts II.B, II.B.2.

⁴⁶ See generally *Alliance for Natural Health U.S. v. Sebelius*, 714 F. Supp. 2d 48 (D.D.C. 2010); *Caronia*, 576 F. Supp. 2d at 385; *Caputo*, 288 F. Supp. 2d at 912; *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000); *Complaint, Allergan, Inc. v. United States*, No. 09 Civ. 1879 (D.D.C. filed Oct. 1, 2009); see generally *infra* Parts II.C.1–II.C.4.

⁴⁷ U.S. CONST. amend. I.

⁴⁸ *Va. State Bd. of Pharmacy*, 425 U.S. at 761.

⁴⁹ See, e.g., *Valentine v. Chrestensen*, 316 U.S. 52, 54 (1942) (finding “the Constitution imposes no . . . restraint on government as respects purely commercial advertising”).

⁵⁰ *Va. State Bd. of Pharmacy*, 425 U.S. at 773 (“What is at issue is whether a State may completely suppress the dissemination of concededly truthful [commercial] information about entirely lawful activity, fearful of that information’s effect upon its disseminators and its recipients. . . . [W]e conclude that the answer to this [question] is in the negative.”).

advertising of drug prices by pharmacies.⁵¹ Eschewing the paternalistic argument that the petitioner had an interest in protecting “unwitting customers” from opting for “low-cost, low-quality service,”⁵² the Court noted that the consumer, seller, and society at large had an interest in the “free flow of commercial information” that “may be as keen, if not keener by far, than [the] interest in the day’s most urgent political debate.”⁵³

On the heels of *Virginia Board of Pharmacy*, the Supreme Court developed a test for determining whether commercial speech received First Amendment protection.⁵⁴ In *Central Hudson Gas & Electric Corporation v. Public Service Commission of New York*, the Court struck down a ban on advertisements by electric utility services,⁵⁵ in part because respondent’s reasons for the ban reflected its fear that the advertisements would needlessly increase energy consumption and costs.⁵⁶ Echoing its sentiments in *Virginia Board of Pharmacy*, the Court rejected the government’s inherently paternalistic suppression of commercial speech.⁵⁷ The Court set forth a four-prong test for assessing the constitutionality of governmental restrictions on commercial speech:⁵⁸ the speech (1) “must concern lawful activity and not be misleading.”⁵⁹ However, the government may ban truthful, non-misleading speech if: (2) the asserted governmental interest in suppressing the

⁵¹ *Id.* at 762.

⁵² *Id.* at 769.

⁵³ *Id.* at 763.

⁵⁴ *See generally* *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm’n N.Y.*, 447 U.S. 557 (1980).

⁵⁵ *Id.* at 561.

⁵⁶ *Id.* at 560–61.

⁵⁷ *See, e.g., id.* at 562; *see also id.* at 574–75 (Brennan, J., concurring) (noting that the restriction at issue was “a covert attempt [by the state] to manipulate the choices of its citizens, not by persuasion or direct regulation, but by depriving the public of the information needed to make a free choice. . . . If the First Amendment guarantee means anything, it means that, absent clear and present danger, government has no power to restrict expression because of the effect its message is likely to have on the public”).

⁵⁸ *See id.* at 566.

⁵⁹ *Id.*

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speech is substantial;⁶⁰ (3) the regulation directly advances the substantial governmental interest; and (4) the restriction on speech is not “more extensive than is necessary to serve that interest.”⁶¹

The *Central Hudson* test was refined and fortified in *44 Liquormart v. Rhode Island*, in which an unanimous Court struck down a Rhode Island prohibition on advertising liquor prices because the regulation failed to satisfy the fourth prong of the *Central Hudson* test.⁶² Although the Court was divided in its reasoning, Justice Thomas, concurring, expressed clear disapprobation for the regulation’s attempts to control consumer choice through the suppression of truthful, non-misleading commercial speech; he argued that if paternalism provides the sole support for a challenged regulation, application of the *Central Hudson* test should be unnecessary, as the law is “per se illegitimate.”⁶³ It is clear that “the Supreme Court looks askance at restrictions on commercial speech imposed for paternalistic purposes.”⁶⁴

*B. Statutory and Regulatory Framework of Off-Label
Promotion*

The FDA exercises authority over the production, sale, and marketing of pharmaceutical products, pursuant to the Federal

⁶⁰ *Id.*

⁶¹ *Id.*

⁶² *44 Liquormart v. Rhode Island*, 517 U.S. 484, 486 (1996) (striking down the regulations because Rhode Island “failed to establish the requisite ‘reasonable fit’ between its regulation and its goal”).

⁶³ *Id.* at 518 (Thomas, J., concurring) (“In cases such as this, in which the government’s asserted interest is to keep legal users of a product or service ignorant in order to manipulate their choices in the marketplace, the balancing test adopted in [*Central Hudson*] should not be applied, in my view. Rather, such an ‘interest’ is per se illegitimate and can no more justify regulation of ‘commercial’ speech than it can justify regulation of ‘noncommercial’ speech.”).

⁶⁴ John Kamp, Daniel E. Troy & Elizabeth Alexander, *FDA Marketing v. First Amendment: Washington Legal Foundation Legal Challenges to Off-Label Policies May Force Unprecedented Changes at FDA*, 54 *FOOD & DRUG L.J.* 555, 557 (1999).

Food, Drug, and Cosmetic Act (“FDCA”).⁶⁵ The FDCA mandates that all new drugs must be approved by the FDA as safe and effective, based on extensive clinical and pre-clinical testing for each intended use before introduction to the market.⁶⁶

The FDCA does not, however, directly constrain physicians’ decisions to prescribe drugs off-label.⁶⁷ Congress has not endowed the FDA with the authority to prohibit physicians from prescribing medications off-label.⁶⁸ Rather, the FDA has recognized that

Congress did not intend FDA to interfere with the practice of medicine. Thus, once a product is approved for marketing for a specific use, FDA generally does not regulate how, or for what uses, physicians prescribe [it]. A licensed physician may prescribe a drug for other uses, or in treatments, regimens, or patient populations, that are not listed on the FDA-approved labeling.⁶⁹

Nevertheless, by manipulating the information disseminated to physicians, the FDA exerts substantial control over their prescribing habits.⁷⁰

⁶⁵ Food, Drug & Cosmetic Act, 21 U.S.C.A. §§ 301–99 (2010).

⁶⁶ *See id.* §§ 321, 355, 360m.

⁶⁷ *See id.* § 396 (reflecting Congress’s amendment of the FDCA to clarify that “[n]othing in this chapter shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed [drug] to a patient for any condition or disease within a legitimate health care practitioner-patient relationship”).

⁶⁸ *See id.* This particular provision of FDAMA was enacted in response to the FDA’s assertion that “The [FDCA] provides [the] FDA with explicit regulatory authority over the use of [drugs].” James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions*, 53 FOOD & DRUG L.J. 71, 78 (1998) (quoting Attachment to Letter from FDA to Hon. Joseph Barton, Chairman, Subcomm. on Oversight and Investigation, House Comm. on Commerce (Apr. 14, 1995)).

⁶⁹ Beck & Azari, *supra* note 68, at 78 n.64 (quoting Michael Friedman, Deputy Comm’r for Operations, FDA, Prepared Statement Before the Subcommittee on Human Resources and Intergovernmental Relations of the House Committee on Government Reform and Oversight (Sept. 12, 1996)).

⁷⁰ *See* David M. Fritch, *Speak No Evil, Hear No Evil, Harm the Patient?: Why the FDA Needs to Seek More, Rather Than Less, Speech From Drug Manufacturers On Off-Label Drug Treatments*, 9 MICH. ST. U. J. MED & L. 315, 336 (2005) (“While the FDA lacks direct authority to directly impose limitations

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Within the drug approval process, the FDA retains authority over the labeling of the drug.⁷¹ A drug's label must detail its risks, benefits, and adequate instructions for use.⁷² The FDA only approves a drug for sale if its labeling conforms to the FDA's specifications.⁷³ "Labeling" is a term of art, which, in addition to physical labels affixed to the drug's packaging, encompasses all written, printed, or graphic material "accompanying" the drug.⁷⁴ "Accompanying" includes not only materials physically associated with the distribution of the drug itself, but all materials supplementing or explaining the product.⁷⁵ According to the FDA's own interpretation of the scope of its power, the term "labeling" encompasses nearly every form of manufacturer communication.⁷⁶ The FDA has also adopted an expansive definition of promotion to include nearly every interpersonal contact between representatives of pharmaceutical manufacturers and prescribers or the public at large.⁷⁷

It is unlawful for the manufacturer to introduce a "misbranded" or "adulterated" drug into interstate commerce.⁷⁸ A drug is

on physicians' prescribing habits, its ability to limit the dissemination of information regarding off-label uses to prescribing physicians represents a significant indirect control over how physicians prescribe medications.").

⁷¹ See 21 U.S.C.A. § 352(f).

⁷² See, e.g., *id.*

⁷³ *Id.* §§ 331(a), (d).

⁷⁴ *Id.* §§ 321(k-m).

⁷⁵ *Kordel v. United States*, 335 U.S. 345, 349-50 (1948).

⁷⁶ 21 C.F.R. § 202.1(l)(1-2) (2010) (defining "labeling" as "[b]rochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, motion picture films, film strips, lantern slides, sound recordings, exhibits, literature, and reprints, and similar pieces of printed, audio, or visual matter descriptive of a drug and references published (for example, the Physicians' Desk Reference)" and promotional materials).

⁷⁷ See Joseph Leghorn, Elizabeth Brophy & Peter V. Rother, *The First Amendment and FDA Restrictions on Off-Label Uses: The Call for a New Approach*, 63 FOOD & DRUG L.J. 391, 394 (2008) (identifying "certain company-supported scientific or educational activities," "initiation of person-to-person contact between sales representatives and prescribers," "direct-to-consumer advertisements," and "improper dissemination of information about an investigational drug during a clinical trial" as promotional activities).

⁷⁸ 21 U.S.C.A. § 331.

misbranded or adulterated if its labeling is “false or misleading in any particular”⁷⁹ or if it includes information regarding a use not approved by the FDA.⁸⁰ Promotion of a drug in a manner inconsistent with its labeling results in the drug being “misbranded.”⁸¹ Because the FDA approves drugs for specific uses, promotional activity that covers uses which are not included in the label, or “off-label” promotion, is a form of misbranding⁸² and is prohibited.⁸³ The FDA is empowered to enjoin manufacturers who promote drugs for off-label uses,⁸⁴ to seize those drugs,⁸⁵ and in some cases, to seek criminal sanctions.⁸⁶

The prohibition is absolute, banning not only fraudulent and untruthful marketing activity, but truthful, non-misleading information as well.⁸⁷ The FDA’s sweeping prohibition of off-label promotion has drawn significant criticism on constitutional grounds.⁸⁸ First, it constitutes a restriction on who may speak,⁸⁹

⁷⁹ *Id.* § 352(a).

⁸⁰ *Id.* § 351.

⁸¹ *Id.*

⁸² *Id.* §§ 351–52 (2006). Off-label uses include use for a condition not included in the label, use in a patient population for which the drug has not been approved as safe and effective (such as pediatrics), or use in dosages different from those in the label (such as a higher than approved dose, or dosing twice, rather than once, daily). *Id.*

⁸³ 21 C.F.R. § 202.1(e)(4)(i)(a) (2010); Citizen Petition Regarding the Food and Drug Administration’s Policy on Promotion of Unapproved Uses of Approved Drugs and Devices; Request for Comments, 59 Fed. Reg. 59820, 59821 (Nov. 18, 1994).

⁸⁴ 21 U.S.C.A. § 332(a).

⁸⁵ *Id.* § 334(a).

⁸⁶ *Id.* § 333.

⁸⁷ 21 C.F.R. § 202.1(e)(4)(i)(a) (mandating that “[a]n advertisement for a prescription drug . . . shall not recommend or suggest any use that is not in the labeling,” regardless of the veracity of the claims made).

⁸⁸ See generally *WLF I*, 13 F. Supp. 2d 51 (D.D.C. 1998); 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 (2010); Frederick R. Ball, Erin M. Duffy & Nina L. Russakoff, *The First Amendment and Off-Label Promotion: Why the Court in United States v. Caronia Got it Wrong*, 2009 BENDER’S HEALTHCARE L. MONTHLY 1 (2009); Fritch, *supra* note 70, at 315; A. Elizabeth Blackwell & James M. Beck, *Drug*

because physicians may freely discuss amongst themselves off-label uses, and may prescribe a medication for any purpose,⁹⁰ yet a manufacturer may not.⁹¹ Second, the restriction on commercial speech is more expansive than necessary to ensure public health and safety.⁹²

C. Legal Challenges to the FDA's Prohibition of Off-Label Promotion

In the past two decades, several legal challenges to the FDA's regulatory scheme have been brought in federal court.⁹³ These lawsuits, while challenging various provisions within the FDA's regulatory framework, all attack the prohibition of off-label promotion as an impermissible abridgement of commercial speech in violation of the First Amendment.⁹⁴ Constitutional challenges to this commercial speech restriction have met with mixed results,

Manufacturers' First Amendment Right to Advertise and Promote Their Products for Off-Label Use: Avoiding a Pyrrhic Victory, 58 FOOD & DRUG L.J. 439 (2003).

⁸⁹ See *infra* Part III.B.1.

⁹⁰ Viagra, for example, is best known for its use in treating erectile dysfunction (ED), but, it was originally approved for use in treating angina—chest pain associated with cardiac disease. Its discovery and success as an ED drug hails from what was originally an off-label use. See Fritch, *supra* note 70, at 319 n.9 (citations omitted). Efficacy has also been demonstrated for other off-label uses, including treating premature babies with under-developed lungs. See *id.* Another example can be found in verapamil, a calcium-channel blocker FDA-approved for treatment of heart disease. Physicians find them to be efficacious for treating headaches, including migraines, yet the FDA has not approved them for treatment of headaches. See Daniel B. Klein & Alexander Tabarrok, *Do Off-Label Drug Practices Argue Against FDA Efficacy Requirements?*, 67 AM. J. ECON. & SOCIOLOGY 743, 756 (2008).

⁹¹ See generally 21 U.S.C.A. §§ 351–52; 21 C.F.R. § 202.1(e)(4)(i)(a).

⁹² See *infra* Part III.D.2.

⁹³ See generally *infra* Parts II.C.1–II.C.4; Alliance for Natural Health, U.S. v. Sebelius, 714 F. Supp. 2d 48 (D.D.C. 2010); United States v. Caronia, 576 F. Supp. 2d 385, 389 (E.D.N.Y. 2008); United States v. Caputo, 288 F. Supp. 2d 912, 921 (N.D. Ill. 2003); *WLF I*, 13 F. Supp. 2d 51; Complaint, *Allergan*, *supra* note 46.

⁹⁴ See *supra* note 93.

leaving the status of the FDA's prohibition of off-label promotion very much unsettled.

1. Washington Legal Foundation

The first challenge to the FDA's policies came in 1997, and concerned two guidance documents restricting (1) dissemination of peer-reviewed scientific journal articles and textbooks by manufacturers and (2) manufacturer-sponsored continuing medical education programs ("CMEs").⁹⁵ The Washington Legal Foundation ("WLF")⁹⁶ sought to enjoin the FDA from enforcing these policies on free speech grounds.⁹⁷ After determining that off-label promotion constituted commercial speech, the district court applied the *Central Hudson* test.⁹⁸ The court found that the speech at issue was truthful and not inherently misleading.⁹⁹ Although the court recognized that the government had a substantial interest in protecting public health and safety by incentivizing manufacturers to seek FDA approval for off-label uses,¹⁰⁰ which was directly advanced by the challenged regulations,¹⁰¹ it nevertheless declared the FDA's policies unconstitutional because it found the restriction on speech to be more extensive than necessary.¹⁰² The court found that there were less restrictive alternatives available, including a

⁹⁵ See Final Guidance on Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64,074 (Dec. 3, 1997) [hereinafter Final Guidance Regulation]; Advertising and Promotion; Guidances, 61 Fed. Reg. 52,800 (1996).

⁹⁶ The Washington Legal Foundation is "a nonprofit public interest law and policy center that defends 'the rights of individuals and businesses to go about their affairs without undue influence from government regulators.'" *WLF I*, 13 F. Supp. 2d at 54 (internal citations omitted); Wash. Legal Found., *WLF Mission*, WASH. LEGAL FOUND., <http://www.wlf.org/org/mission.asp> (last visited Apr. 8, 2011).

⁹⁷ *WLF I*, 13 F. Supp. 2d at 54.

⁹⁸ *Cent. Hudson Gas & Elec. Co. v. Pub. Serv. Comm'n N.Y.*, 447 U.S. 557, 567 (1980); see *supra* Part II.A.

⁹⁹ *WLF I*, 13 F. Supp. 2d at 65–69.

¹⁰⁰ *Id.* at 69–71.

¹⁰¹ *Id.*

¹⁰² *Id.* at 72–74.

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“full, complete, and unambiguous disclosure by the manufacturer” that the advocated use is off-label and not FDA approved.¹⁰³ Faced with such disclosure, “[a] physician would be immediately alerted to the fact that the ‘substantial evidence standard’ had not been satisfied, and would evaluate the communicated message accordingly.”¹⁰⁴

After the decision in *WLF I*, the Food and Drug Administration Modernization Act of 1997 (“FDAMA”) took effect.¹⁰⁵ Within FDAMA, the very policies declared unconstitutional in *WLF I* were codified in section 401.¹⁰⁶ In a separate decision, *WLF II*,¹⁰⁷ the district court *sua sponte* extended its *WLF I* ruling to apply to section 401 of FDAMA, declared that section unconstitutional, and enjoined the FDA from enforcing it.¹⁰⁸

On appeal, the FDA disclaimed its original argument that FDAMA authorized the FDA to regulate or prohibit speech,¹⁰⁹ stating instead that “in its view, neither the FDAMA nor the CME guidance independently authorizes the FDA to prohibit or sanction speech.”¹¹⁰ At oral argument the FDA elected to interpret section 401 as providing a “safe harbor,” that ensures that certain types of conduct would not be used against manufacturers in criminal actions for misbranding.¹¹¹ It insisted, however, that FDAMA permitted criminal sanctions against any manufacturer who completely disregarded section 401’s conditions on off-label promotion “provides that a manufacturer who disregards [section

¹⁰³ *Id.* at 73; *see also id.* 68–69.

¹⁰⁴ *Id.* at 73.

¹⁰⁵ Food & Drug Administration Modernization Act, Pub L. No. 105-115 (1997) (codified at 21 U.S.C.A. § 360aaa (West 2010)).

¹⁰⁶ *See Wash. Legal Found. v. Henney (WLF II)*, 56 F. Supp. 2d 81, 87 (1999).

¹⁰⁷ *See generally id.* The opinion in *WLF II* was necessitated after the government sought declaratory relief from the *WLF I* court that the court’s ruling did not apply to section 401 of FDAMA. *Id.* at 83–84.

¹⁰⁸ *Id.* at 88–89.

¹⁰⁹ *See WLF III*, 202 F.3d 331, 335 (2000).

¹¹⁰ *Id.*

¹¹¹ *Id.* at 335.

401J]’s conditions . . . might be liable in some fashion.”¹¹² The FDA’s new interpretation brought its position in line with WLF’s, eliminating the controversy.¹¹³ The D.C. Circuit lamented the lost opportunity to resolve “a difficult constitutional question of considerable practical importance” and noted that, because of the FDA’s concession, “the dispute between the parties has disappeared before our eyes.”¹¹⁴ It vacated the *WLF I* and *WLF II* rulings for want of controversy.¹¹⁵ In the wake of *WLF III*, the FDA interpreted the Circuit’s ruling to mean that the “FDA, consistent with its longstanding interpretation of the laws it administers, may proceed, on a case-by-case basis, to determine from a manufacturer’s written materials and activities how it intends that its products be used.”¹¹⁶ Although the *WLF* decisions addressed only a narrow subset of off-label speech—distribution of scientific literature and sponsorship of CMEs¹¹⁷—the district court’s vacated opinions influenced subsequent decisions addressing the constitutionality of restrictions on off-label promotion.¹¹⁸

2. *United States v. Caputo*

In 2003, the FDA’s prohibition of off-label promotion faced another constitutional challenge.¹¹⁹ In *United States v. Caputo*, the defendants challenged the FDA’s prohibition of off-label promotion of a medical device.¹²⁰ The district court largely

¹¹² *Id.*

¹¹³ *Id.*

¹¹⁴ *Id.*

¹¹⁵ *Id.* at 336.

¹¹⁶ *WLF III* Decision Notice, *supra* note 17.

¹¹⁷ See Final Guidance Regulation, *supra* note 95; Advertising and Promotion, *supra* note 95.

¹¹⁸ See, e.g., *United States v. Caputo*, 288 F. Supp. 2d 912, 921–22 (N.D. Ill. 2003) (adopting the reasoning of the *WLF* district court).

¹¹⁹ See generally *id.*

¹²⁰ *Id.* at 912. This case is notable for *Caputo*’s particularly egregious marketing behavior and disregard for FDA regulations, see *id.* at 915–16; however the holding and analysis ultimately affect all manufacturers, regardless

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adopted *WLF I*'s reasoning, but departed from *WLF I* in holding that the prohibition was constitutional.¹²¹ In addressing the FDA's interest in restricting speech, the court reasoned that "[p]ermitting manufacturers to promote off-label uses would completely undermine the government's interest in subjecting off-label uses to the FDA's evaluation process as well as the government's interest in preserving the FDCA's new drug approval process."¹²²

Distinguishing the promotion at issue in *Caputo* from the dissemination of academic writing and sponsorship of CMEs in *WLF I*, *Caputo* found prohibition of all off-label promotion—even that which is truthful and non-misleading—to be constitutional because “permitting Defendants to engage in all forms of truthful, non-misleading promotion of off-label use would severely frustrate the FDA's ability to evaluate the effectiveness of off-label uses.”¹²³ Because the court could not envision a less restrictive means of achieving this interest, it preserved the FDA's authority to prohibit off-label commercial speech.¹²⁴ On appeal, the Seventh Circuit did not resolve the First Amendment quandary, and declared that it “[f]ortunately . . . need not decide today whether a seller of drugs . . . has a constitutional right to promote off label uses,”¹²⁵ affirming *Caputo* on more narrow grounds.¹²⁶

3. *Allergan*

More recently, the FDA commenced a barrage of civil and criminal sanctions against the manufacturer Allergan, Inc. for alleged off-label marketing of its pharmaceutical product, Botox.¹²⁷ Allergan fought back, filing a civil suit challenging the

of their culpability.

¹²¹ *Id.* at 921–22.

¹²² *Id.* at 921.

¹²³ *Id.* at 922.

¹²⁴ *Id.*

¹²⁵ *United States v. Caputo*, 517 F.3d 935, 940 (7th Cir. 2008).

¹²⁶ *See id.* at 941 (declining to proceed with a *Central Hudson* analysis because, given the particularly egregious marketing endeavors of Mr. Caputo, “[t]here was no lawful activity . . . to promote”).

¹²⁷ *See Information*, *United States v. Allergan, Inc.*, No. 10 Cr. 375 (N.D.

constitutionality of the prohibition on First Amendment grounds.¹²⁸ With the threat of massive civil and criminal penalties looming, Allergan was permitted to plead guilty and settle the civil complaints, conditioned upon abandonment of its First Amendment suit.¹²⁹ The settlement left the question of the constitutionality of the FDA's prohibitions unanswered.

4. Caronia's First Amendment Challenge

The FDA investigated alleged off-label promotion of Xyrem by Jazz Pharmaceuticals, resulting in the indictment of Caronia on two misdemeanor counts:¹³⁰ (1) conspiracy to misbrand Xyrem by marketing it to the undercover informant-physician for off-label uses;¹³¹ and (2) misbranding a drug held for sale in interstate commerce.¹³² Caronia moved to dismiss the charges because, *inter*

Ga. Sept. 1, 2010); Complaint, United States *ex rel.* Hallivis v. Allergan, Inc., No. 09 Civ. 3434 (D. Md. Oct. 26, 2009); Complaint, United States *ex rel.* Beilfuss v. Allergan, Inc., No. 08 Civ. 1883 (D. Mass. May 27, 2008); Complaint, United States *ex rel.* Lang v. Allergan, Inc., No. 07 Civ. 1288 (N.D. Ga. June 5, 2007).

¹²⁸ Complaint, *Allergan*, *supra* note 46.

¹²⁹ See Press Release, Allergan, Inc., Allergan Resolves United States Government Investigation of Past Sales and Marketing Practices Relating to Certain Therapeutic Uses of Botox® (Sept. 1, 2010), available at http://pdfserver.amlaw.com/cc/Allergan_settlement090110.pdf ("To resolve the criminal and civil investigation, *Allergan was required by the Government to dismiss Allergan's First Amendment lawsuit . . .* in which Allergan sought a ruling that it could proactively share truthful scientific and medical information with the medical community to assist physicians in evaluating the risks and benefits [of off-label uses of Botox]."(emphasis added)); see also Press Release, Dep't of Justice, Allergan Agrees to Plead Guilty and Pay \$600 Million to Resolve Allegations of Off-Label Promotion of Botox® (Sept. 1, 2010), available at <http://www.justice.gov/opa/pr/2010/September/10-civ-988.html>.

¹³⁰ United States v. Caronia, 576 F. Supp. 2d 385, 389 (E.D.N.Y. 2008).

¹³¹ *Id.*; see Food, Drug & Cosmetic Act, 21 U.S.C.A. §§ 331(a) & (k) (West 2010); Violent Crime Control & Law Enforcement Act of 1994, 18 U.S.C.A. § 371 (West 2010).

¹³² *Caronia*, 576 F. Supp. 2d at 389. See 21 U.S.C.A. §§ 331(k) & 331(a)(1).

alia, the misbranding provisions violated his free speech rights.¹³³ The court found that the off-label promotion constituted commercial speech,¹³⁴ and that the provisions did not violate the First Amendment.¹³⁵

Under *Central Hudson*, the threshold question is not whether the *speech* itself is unlawful: such a test would present a closed tautology;¹³⁶ the question is whether the *conduct urged by the speech* is unlawful.¹³⁷ Relying on *WLF I*, *Caronia* held that, because physicians may prescribe Xyrem for off-label uses, *Caronia*'s speech did not concern unlawful activity,¹³⁸ and that the statements were not inherently misleading.¹³⁹ Adopting the reasoning of *WLF I* and *Caputo*, *Caronia* found that physicians receiving *Caronia*'s speech were generally aware of the FDA-approval process and its implications, and could adequately evaluate the validity of their claims: the *Caronia* court wrote "[g]iven the sophistication of the audience to whom the off-label uses were promoted, this Court cannot conclude . . . that

¹³³ *Caronia*, 576 F. Supp. 2d at 393.

¹³⁴ *Id.* at 396. The court noted that:

regardless what else might have been covered in his discussions, *Caronia*'s alleged speech was made on behalf of the manufacturer and clearly (1) encouraged physicians to prescribe Xyrem, (2) referred to a specific product, and (3) was economically motivated. Any such promotion by *Caronia* to physicians on behalf of Xyrem's manufacturer of the drug's off-label uses would be commercial speech and be "entitled to the qualified but nonetheless substantial protection accorded to commercial speech."

Id. (citing *Bolger v. Young Drug Prods. Co.*, 463 U.S. 60, 68 (1983)).

¹³⁵ *Id.* at 402.

¹³⁶ See *WLF I*, 13 F. Supp. 2d 51, 66 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000) (rejecting the FDA's argument that off-label speech concerns unlawful activity because off-label promotion violates federal law).

¹³⁷ 44 *Liquormart v. Rhode Island*, 517 U.S. 484, 497 n.7 (1996) ("[T]he First Amendment does not protect speech *about unlawful activities*." (emphasis added)).

¹³⁸ *Caronia*, 576 F. Supp. 2d at 397–98.

¹³⁹ *Id.*

[Caronia's] speech was inherently misleading."¹⁴⁰

Turning to the second prong of the *Central Hudson* test, *Caronia* found, relying on *WLF I*, that restricting off-label promotion served a substantial government interest.¹⁴¹ *Caronia* acknowledged the substantial government interest in protecting the health and the public¹⁴² and that, in order to attain that objective, the government had "a substantial interest in compelling manufacturers to get off-label treatments on-label."¹⁴³ In addressing the third prong of the *Central Hudson* test, and relying yet again on *WLF I* and *Caputo*, the *Caronia* court ruled that prohibition of off-label promotion directly advanced the "substantial government interest in requiring manufacturers to submit supplemental applications to obtain FDA approval for new uses of previously approved drugs."¹⁴⁴

Finally, addressing the fourth prong of the *Central Hudson* test—whether the prohibition is only as extensive as is necessary to further the government's interest¹⁴⁵—the court distinguished *WLF I*, which concerned only a limited form of off-label speech.¹⁴⁶ The *Caronia* court failed to recognize the *WLF I* finding that a less restrictive alternative to absolute prohibition existed: namely, "full, complete, and unambiguous disclosure by the manufacturer of its involvement in the subject activities and the fact that the uses discussed were off-label,"¹⁴⁷ and relied instead on *WLF I* dicta that

¹⁴⁰ *Id.* (internal quotation marks and citations omitted) (citing *United States v. Caputo*, 288 F. Supp. 2d 912, 921 (N.D. Ill. 2003)).

¹⁴¹ *Id.* at 398.

¹⁴² *Id.*

¹⁴³ *Id.*; accord *Caputo*, 288 F. Supp. 2d at 921; *WLF I*, 13 F. Supp. 2d 51, 72 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000) ("[O]ne of the few mechanisms available to the FDA to compel manufacturer behavior [with regard to ensuring the safety of new uses for drugs] is to constrain marketing options; i.e. control labeling, advertising, and marketing.").

¹⁴⁴ *Caronia*, 576 F. Supp. 2d at 398.

¹⁴⁵ *Cent. Hudson Gas & Elec. Co. v. Pub. Serv. Comm'n N.Y.*, 447 U.S. 557, 569–70 (1980).

¹⁴⁶ See *WLF I*, 13 F. Supp. 2d at 54; see also Final Guidance Regulation, *supra* note 95; Advertising and Promotion, *supra* note 95.

¹⁴⁷ *Caronia*, 576 F. Supp. 2d at 399 (citing *WLF I*, 13 F. Supp. 2d at 57–58).

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“[w]ere manufacturers permitted to engage in all forms of marketing of off-label treatments, a different result might be compelled.”¹⁴⁸ Instead, it relied on *Caputo*’s finding that a First Amendment challenge to the off-label prohibition threatened the FDA’s ability to control and prohibit manufacturer’s off-label promotion.¹⁴⁹ Noting that no less restrictive means of advancing the government’s interest was identified in *Caputo*,¹⁵⁰ *Caronia* concluded that “the prohibitions . . . pass constitutional muster under the fourth prong of *Central Hudson*.”¹⁵¹

III. *CITIZENS UNITED*: FROM POLITICAL SPEECH TO COMMERCIAL SPEECH

The Supreme Court’s holding in *Citizens United v. F.E.C.* has garnered significant criticism for its implications for corporate participation in political discourse.¹⁵² However, the Court’s reasoning in striking down the FEC’s regulatory scheme¹⁵³ may impact other areas of heavily regulated speech, including some forms of commercial speech, such as the off-label promotion of prescription pharmaceuticals.

¹⁴⁸ *Id.* (second emphasis added).

¹⁴⁹ *United States v. Caputo*, 288 F. Supp. 2d 912, 922 (N.D. Ill. 2003).

¹⁵⁰ *Caronia*, 576 F. Supp. 2d at 399 (citing *Caputo*, 288 F. Supp. 2d at 922).

¹⁵¹ *Id.* at 401–02 (“[T]his Court is unable to identify non-speech restrictions that would likely constrain in any effective way manufacturers from circumventing [the FDA’s] approval process.” (citing *Caputo*, 288 F. Supp. 2d at 922)).

¹⁵² *See, e.g.*, Dworkin, *supra* note 19, at 39 (reporting the *Citizens United* decision arose from the Court’s political preference for the Republican Party and/or its general favoritism of corporate interests); Walker Wilson, *supra* note 19, at 2368–69; Liptak, *supra* note 19, at A1; Barack Obama, Remarks by the President in the State of the Union Address (Jan. 27, 2010) (“[L]ast week, the Supreme Court reversed a century of law to open the floodgates for special interests—including foreign companies—to spend without limit in our elections Well, I don’t think American elections should be bankrolled by America’s most powerful interests, and worse, by foreign entities.”).

¹⁵³ *Citizens United v. F.E.C.*, 130 S. Ct. 876, 896 (2010).

A. The Citizens United Decision

In January 2008, Citizens United, a non-profit organization, aired *Hillary: the Movie*¹⁵⁴ that criticized then-Senator Hillary Clinton,¹⁵⁵ and sought to dissuade voters from electing her as the Democratic candidate for President.¹⁵⁶ Citizens United wanted to make the film available via online video-on-demand in the days leading to the 2008 primary.¹⁵⁷ It feared, however, it might violate section 441b of the Bipartisan Campaign Reform Act,¹⁵⁸ which prohibited corporations and unions from using general treasury funds to finance advocacy for the election or defeat of a candidate.¹⁵⁹ Citizens United sought a declaratory judgment that it could air *Hillary*, as well as injunctive relief against the FEC in a District of Columbia trial court.¹⁶⁰ That court granted summary judgment in favor of the FEC, finding the law constitutional, both facially and as applied to Citizens United.¹⁶¹ The Supreme Court heard the appeal directly, and held section 441b's prohibition of corporate electioneering unconstitutional.¹⁶² Writing for the Court, Justice Kennedy called the FEC's ambiguous regulatory scheme an "unprecedented governmental intervention into the realm of speech."¹⁶³

¹⁵⁴ *Id.* at 886–87.

¹⁵⁵ *Id.* at 887 (“[T]o promote the film, [Citizens United] produced two 10-second ads and one 30-second ad for Hillary. Each ad includes a short (and in our view, pejorative) statement about Senator Clinton.”).

¹⁵⁶ *Id.* at 888.

¹⁵⁷ *Id.* at 887–88.

¹⁵⁸ *Id.* at 887.

¹⁵⁹ See Bipartisan Campaign Reform Act, 2 U.S.C.A. § 441b(b)(2) (West 2010).

¹⁶⁰ *Citizens United*, 130 S. Ct. at 888.

¹⁶¹ *Id.*

¹⁶² *Id.* at 913; see 2 U.S.C. § 441b.

¹⁶³ *Citizens United*, 130 S. Ct. at 896.

B. But Is It Unprecedented? Citizens United and Off-Label Promotion

A regulatory scheme analogous to the regulation of corporate political speech found unconstitutional in *Citizens United* exists in the prohibition of off-label promotion.¹⁶⁴ An examination of the parallels between the FDA's regulation of off-label promotion and the FEC's regulation of corporate political speech reveals that the FDA's regulation should fail under the principles set forth in *Citizens United*.

1. The FDA's Prohibition of Off-Label Promotion By Manufacturers, Like the Prohibitions in Citizens United, Constitutes a Restriction On Who May Speak

Citizens United recognized that the ban on corporate independent expenditures constituted a restriction on who may speak.¹⁶⁵ In terms reaching more broadly than political speech alone, the Court noted that:

[p]remised on mistrust of governmental power, the First Amendment stands against attempts to disfavor certain subjects or viewpoints. Prohibited too are restrictions *distinguishing among different speakers*, allowing speech by some but not others. As instruments to censor, these categories are interrelated: speech restrictions based on the identity of the speaker are all too often simply a means to control content.¹⁶⁶

The Court continued, finding that if the regulation applied to individuals, not corporations, engaged in political advocacy, "no one would believe that it is merely a time, place, or manner restriction on speech. Its purpose and effect are to silence entities whose voices the Government deems to be suspect."¹⁶⁷

Likewise, the FDA's prohibition of off-label promotion is a

¹⁶⁴ See *supra* Part II.B.

¹⁶⁵ *Citizens United*, 130 S. Ct. at 898–99.

¹⁶⁶ *Id.* (emphasis added).

¹⁶⁷ *Id.* at 898.

restraint based upon government mistrust of a particular speaker. Believing, rightly or wrongly, that a manufacturer may attempt to persuade physicians to prescribe their drug, and believing, rightly or wrongly, that such a speech is harmful,¹⁶⁸ the FDA severely limits the ways in which manufacturers may discuss with physicians truthful, non-misleading, peer-reviewed scientific or medical journal articles related to an off-label use.¹⁶⁹ Yet that discussion between two physicians, when each is unaffiliated with a pharmaceutical company, is fully protected scientific speech entitled to the highest First Amendment protection.¹⁷⁰ When the manufacturer or its agent speaks, however, the same speech magically transforms into commercial speech¹⁷¹—the red-headed stepchild of First Amendment jurisprudence¹⁷²—and the manufacturer may face criminal liability.¹⁷³ The facts of *Caronia* make the disparity clear: Dr. Gleason became the first physician ever prosecuted under the misbranding statutes¹⁷⁴ because he spoke about an off-label use of a drug on behalf of its manufacturer.¹⁷⁵

¹⁶⁸ *But see infra* Parts VI.A & B.

¹⁶⁹ *See* Food, Drug & Cosmetic Act, 21 U.S.C.A. §§ 301–99 (West 2010); GOOD REPRINT PRACTICES, *supra* note 16, § II.

¹⁷⁰ *See* *Bracco Diagnostics, Inc. v. Amersham Health, Inc.*, 627 F. Supp. 2d 384, 458 (D.N.J. 2009) (citing *WLF I*, 13 F. Supp. 2d 51, 63 (D.D.C. 1998)); *WLF I*, 13 F. Supp. 2d at 63 (noting that “[i]t is beyond dispute that when considered outside of the context of manufacturer promotion of their drug products, CME seminars, peer-reviewed medical journal articles and commercially-available medical textbooks merit the highest degree of constitutional protection” because “[s]cientific and academic speech reside at the core of the First Amendment”).

¹⁷¹ *See* *United States v. Caronia*, 576 F. Supp. 2d 385, 395–96 (E.D.N.Y. 2008); *WLF I*, 13 F. Supp. 2d at 62–65. *See also, generally*, *United States v. Caputo*, 288 F. Supp. 2d 912 (N.D. Ill. 2003) (failing to even consider whether off-label promotion constitutes commercial speech before commencing a *Central Hudson* analysis).

¹⁷² *See* *Ohralik v. Ohio State Bar Ass’n*, 436 U.S. 447, 456 (1978) (noting that commercial speech receives “a limited measure of protection, commensurate with its subordinate position in the scale of First Amendment values” (emphasis added)).

¹⁷³ 21 C.F.R. § 202.1(k) (2010).

¹⁷⁴ *Judge Strikes Down First Amendment Arguments*, *supra* note 10, at 9.

¹⁷⁵ *Id.*

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Had he instead discussed the same topic, made the same recommendations, and said the same exact words while at a casual dinner with a colleague, no criminal sanctions would attach.¹⁷⁶ That speech regarding off-label uses of a drug becomes criminal only when a manufacturer speaks makes the constitutional infirmity of the FDA's regulation pellucid.

2. *Under Citizens United, the FDA's Ambiguous Regulatory Scheme Functions Like a Prior Restraint on Speech*

Citizens United identified section 441b as “an outright ban [on speech], backed by criminal sanctions.”¹⁷⁷ Acknowledging that the ban does not constitute a prior restraint on speech in the traditional sense,¹⁷⁸ the Court noted that “[a]s a practical matter, however, given the complexity of the regulations and the deference courts show to administrative determinations, a speaker who wants to avoid the threats of criminal liability and the heavy costs of defending against FEC must ask a governmental agency for prior permission to speak.”¹⁷⁹ That is, a corporation could not discern whether its proposed speech was lawful from the perplexing regulatory scheme cobbled together by the FEC, and was therefore forced either to remain silent or to ask the government to pass upon the acceptability of its speech prior to speaking.¹⁸⁰ The FEC, in essence, created a regulatory regime where it could “select what political speech is safe for public consumption by applying ambiguous tests”¹⁸¹ which the Court roundly criticized.¹⁸²

¹⁷⁶ In *Caronia*, the District court was even hesitant to apply the ban to Dr. Gleason—noting his favored status as a physician. See *Caronia*, 576 F. Supp. 2d at 395–96.

¹⁷⁷ *Citizens United v. F.E.C.*, 130 S. Ct. 876, 897 (2010).

¹⁷⁸ *Id.* at 895 (noting that “prospective speakers are not compelled by law to seek an advisory opinion from the FEC before the speech takes place” (emphasis added)).

¹⁷⁹ *Id.* at 896 (citing Bipartisan Campaign Reform Act 2 U.S.C.A. § 437(f) (West 2010)) (equating the regulation to “licensing laws implemented in the 16th- and 17th century England, laws and governmental practices of the sort that the First Amendment was drawn to prohibit”).

¹⁸⁰ See *id.* (citing 2 U.S.C. § 437(f)).

¹⁸¹ *Id.* at 896. The Supreme Court held that “[t]he Government may

The complexity of the FDA's ban of off-label promotion has clear parallels to the regulatory scheme struck down in *Citizens United*. The FDA's regulatory scheme is hopelessly muddled, so as to fail to provide clear guidance as to what promotional activities are permitted. Despite the codification of the FDA's authority in the FDCA¹⁸³ and FDAMA,¹⁸⁴ the FDA continues to disseminate guidance documents containing "amorphous regulatory interpretation";¹⁸⁵ and in so doing it essentially "select[s] what . . . speech is safe for public consumption by applying an ambiguous test."¹⁸⁶ As in *Citizens United*, a regulatory agency—this time the FDA—has constructed an abstruse regulatory scheme that essentially functions as a prior restraint on speech.¹⁸⁷

regulate corporate political speech through disclaimer and disclosure requirements, but it may not suppress that speech altogether." *Id.* at 886.

¹⁸² *Id.* at 895–96 (comparing the FEC's regulatory scheme to the English licensing laws of the 16th and 17th centuries that prompted the ratification of the First Amendment, and describing the ill-effects of such a regulatory scheme on modern free speech).

¹⁸³ See Food, Drug & Cosmetic Act, 21 U.S.C.A. §§ 301–99 (West 2010).

¹⁸⁴ See FDAMA, Pub L. 105-115 (1997) (codified at 21 U.S.C.A. § 360aaa (West 2010)).

¹⁸⁵ *Citizens United*, 130 S. Ct. at 889.

¹⁸⁶ *Id.* at 896.

¹⁸⁷ See *id.* at 895–96. Although commercial speech receives some First Amendment protection, see *supra* Part II.A, the Supreme Court has intimated from the inception of the commercial speech doctrine that some protections available to other speech might be unavailable to commercial speech. In *Virginia State Board of Pharmacy*, Justice Blackmun noted that because "commercial speech *may* be more durable than other kinds [of speech] . . . there is little likelihood of its being chilled by proper regulation and forgone entirely." *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council*, 425 U.S. 748, 772 n.24 (1976) (emphasis added). As a result, "the greater objectivity and hardiness of commercial speech, *may* make it less necessary to tolerate inaccurate statements for fear of silencing the speaker," *id.* (emphasis added), and "*may* also make inapplicable the prohibition against prior restraints." *Id.* (emphasis added). Relying on this equivocal, footnoted statement in *Virginia State Board of Pharmacy*, the *Central Hudson* Court found it would be appropriate to require "a system of previewing advertising campaigns to insure that they will not defeat" governmental objectives. *Cent. Hudson Gas & Elec. Corp. v. Public Serv. Comm'n N.Y.*, 447 U.S. 557, 571 n.13 (1980). The Supreme Court, however, has never definitively held that the doctrine of prior

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In the FDA's most recent interpretation of its own authority to regulate the dissemination of truthful, non-misleading, peer-reviewed scientific journal articles, the infirmity of a *de facto* prior restraint is pellucid.¹⁸⁸ The provision of FDAMA challenged in *WLF II*, section 401,¹⁸⁹ sunsetted in 2006,¹⁹⁰ leaving no guidance as to how, if at all, manufacturers could disseminate journal articles to physicians.¹⁹¹ After three years without guidance, the FDA at last published its "Good Reprint Practices."¹⁹² Riddled with subjective criteria for appropriate dissemination of journal reprints,¹⁹³ it does little to provide adequate guidance. First, the Good Reprint Practices dictate that journal articles must be "distributed separately from information that is promotional in nature," yet nowhere do they define promotional material,¹⁹⁴ and the FDA has previously interpreted promotional material to include "literature [and] reprints."¹⁹⁵ Second, the guidance document states, without explanation, that "[t]he information must not . . . pose a significant risk to public health, if relied upon."¹⁹⁶ Third, it omits the "safe harbor" contained within section 401, as interpreted by the FDA in *WLF III*.¹⁹⁷ It perpetuates, however, the FDA's "interpretation" of *WLF III*'s holding, notwithstanding the fact that the case was mooted for lack of controversy based on the existence

restraint absolutely does not apply to commercial speech.

¹⁸⁸ See GOOD REPRINT PRACTICES, *supra* note 16.

¹⁸⁹ FDAMA, Pub L. No. 105-15, 111 Stat. 2296 (1997) (codified at 21 U.S.C. § 360aaa. (2006)).

¹⁹⁰ GOOD REPRINT PRACTICES, *supra* note 16 § II.

¹⁹¹ See, e.g., Robert I. Field, *The FDA's New Guidance for Off-Label Promotion Is Only a Start*, 33 P&T 220, 220 (2008) (noting that "FDAMA's limitations on off-label promotion expired on September 30, 2006, and Congress has yet to reauthorize them" and that what was, at the time, a draft guidance was "an attempt to fill the void").

¹⁹² See generally GOOD REPRINT PRACTICES, *supra* note 16.

¹⁹³ See generally *id.*

¹⁹⁴ See *id.* § IV. B.

¹⁹⁵ 21 C.F.R. § 202.1(1)(1-2) (2010).

¹⁹⁶ GOOD REPRINT PRACTICES, *supra* note 16 § IV.A.

¹⁹⁷ See Stephen Barlas, *New FDA Guidance on Off-Label Promotion Falls Short for Everyone: Obama Administration Is Likely to Revisit It*, 34 P&T 122, 122 (2009).

of this safe harbor:¹⁹⁸ the guidance document states that the “FDA’s legal authority to determine whether distribution of medical or scientific information constitutes promotion of an unapproved ‘new use’ or whether such activities cause a product to violate the [FDCA] has not changed.”¹⁹⁹ Because the FDA enabled itself, in the wake of *WLF III*, to “proceed, in the context of case-by-case enforcement, to determine whether in the manufacturer’s written materials and activities . . .”²⁰⁰ off-label promotion has occurred, the Good Reprint Practices leaves a manufacturer with no guidance whatsoever as to what it may or may not lawfully do. The manufacturer must either remain silent²⁰¹ or seek clarification—essentially permission—from the FDA to engage in promotional speech.²⁰²

One consideration that led the *Citizens United* Court to declare the FEC’s ban on speech unconstitutional has particular relevance to the FDA’s regulatory scheme. In *Citizens United*, the Court noted that “[w]hen the FEC issues advisory opinions that prohibit speech, ‘[m]any persons, rather than undertake the considerable burden (and sometimes risk) of vindicating their rights through case-by-case litigation, will choose simply to abstain from protected speech.’”²⁰³ The risk of vindicating a corporation’s speech rights through litigation is especially acute in the off-label promotion realm: if a manufacturer is found guilty of criminally misbranding its drug,²⁰⁴ the Health and Human Services Office of the Inspector General (OIG) may preclude the manufacturer from

¹⁹⁸ *WLF III* Decision Notice, *supra* note 17, at 14, 287.

¹⁹⁹ GOOD REPRINT PRACTICES, *supra* note 16 § III.

²⁰⁰ See *WLF III* Decision Notice, *supra* note 17, at 14, 287.

²⁰¹ Cf. *Citizens United v. F.E.C.*, 130 S. Ct. 876, 896 (2010) (noting that the FEC’s regulation of corporate political speech left corporations to choose to remain silent or request permission to speak).

²⁰² Cf. *id.* at 895 (citing 2 U.S.C.A. § 437(f) (2006)) (same).

²⁰³ *Id.* at 896 (citing *Virginia v. Hicks*, 539 U.S. 113, 119 (2003)).

²⁰⁴ See, e.g., *United States v. Caputo* 456 F. Supp. 2d 970 (N.D. Ill. 2006) *aff’d in part, vacated in part* 517 F.3d. 935 (7th Cir. 2008). See also *United States v. Caputo*, 288 F. Supp. 2d 912, 922 (N.D. Ill. 2003) (denying motion to dismiss indictment in part because 21 C.F.R. §801.4 does not offend the First Amendment).

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receiving reimbursement from Medicaid and Medicare for prescriptions of any drug it manufactures.²⁰⁵ Manufacturers “cannot realistically challenge the government in court [on] . . . whether the charges alleged are compatible with the Constitution The risk/reward calculus is skewed dramatically in favor of settlement when a loss would jeopardize the [manufacturer’s] viability by forfeiting government reimbursement for its products.”²⁰⁶

While the similarities between a system of regulatory patchwork and the odious, traditional, form of prior restraint in which “prospective speakers are not compelled by law” to seek permission from the government may not be obvious,²⁰⁷ both systems chill speech in a similar way. The Supreme Court has previously declared unconstitutional regulations that, while not traditionally a prior restraint, function collectively in much the same way.²⁰⁸ In *Bantam Books, Inc. v. Sullivan*, the Court struck down a Rhode Island law designed to shield youth from books that the state considered to be obscene, immoral, or impure.²⁰⁹ The statute enabled the Rhode Island Commission to Encourage Morality in Youth to “investigat[e] situations which may cause . . . undesirable behavior of juveniles . . . [and] recommend legislation, prosecution, and/or treatment that would ameliorate or eliminate said causes.”²¹⁰ The Commission, after having determined that a

²⁰⁵ See Health Care Programs: Fraud and Abuse; Revised OIG Exclusions Authorities Resulting from Public Law 104-191, 63 Fed. Reg. 46,676, 46,686 (Sept. 2, 1998).

²⁰⁶ Osborn, *supra* note 88, at 328 (emphasis added). The result is often astronomical settlement figures from manufacturers with varying degrees of culpability yet uniformly desperate to maintain their financial solvency. See, e.g., Press Release, Dep’t of Justice, Pharm. Giant AstraZeneca to Pay \$520 Million for Off-label Drug Mktg. (Apr. 27, 2010), available at <http://www.justice.gov/opa/pr/2010/April/10-civ-487.html>; Press Release, U.S. Dep’t Health and Human Servs., Justice Dep’t. Announces Largest Health Care Fraud Settlement in its History (Sept. 2, 2009), available at <http://www.hhs.gov/news/press/2009pres/09/20090902a.html> (announcing a \$2.3 Billion settlement).

²⁰⁷ *Citizens United*, 130 S. Ct. at 895.

²⁰⁸ See *Bantam Books, Inc. v. Sullivan*, 372 U.S. 58, 64 (1963).

²⁰⁹ *Id.*

²¹⁰ 1959 R.I. Acts & Resolves 880.

particular book was obscene,²¹¹ sent notices to publishers and bookstores, announcing that the condemned books could not be sold, displayed, or distributed to customers under the age of eighteen and threatening that “[t]he Attorney General will act for us in the case of non-compliance.”²¹² Upon receiving such notice, the petitioners ceased to publish or offer for sale the banned books.²¹³ The Supreme Court found that Rhode Island’s scheme constituted a system of prior restraints²¹⁴ in part because “[t]he distributor [was] left to speculate whether the Commission considers [a] publication obscene or simply harmful to juvenile morality,” and “the ‘cooperation’ [the Commission sought] from distributors invariably entail[ed] the complete suppression of the listed publication.”²¹⁵

IV. FROM CARONIA ONWARD: A ROUTE FORWARD

In conducting its *Central Hudson* analysis, *Caronia* erred in two ways, resulting ultimately in an incorrect ruling on three of the four *Central Hudson* prongs. First, the court too willingly accepted as “substantial” the FDA’s interest in subjecting new uses of medications to FDA approval,²¹⁶ and therefore did not consider the actual interest the FDA is charged with protecting.²¹⁷ Second, this error resulted in *Caronia*’s finding that the regulation served a substantial government interest under *Central Hudson*’s third prong.²¹⁸ Finally, despite acknowledging the consumer savvy of the physicians to whom off-label promotion is directed,²¹⁹ the court

²¹¹ See *Bantam Books*, 372 U.S. at 64. The commission defined “obscene” more broadly than the meaning of obscene under the First Amendment. *Id.*

²¹² *Id.* at 62 n.5.

²¹³ *Id.* at 63.

²¹⁴ *Id.* at 70.

²¹⁵ *Id.* at 71.

²¹⁶ See *United States v. Caronia*, 576 F. Supp. 2d 385, 398 (E.D.N.Y. 2008).

²¹⁷ See *infra* Part VI.A.

²¹⁸ See *infra* Part IV.B.

²¹⁹ See *Caronia*, 576 F. Supp. 2d at 397–98.

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errantly followed the flawed reasoning of *Caputo*,²²⁰ failing to find a less speech-restrictive alternative to absolute prohibition of an entire class of commercial speech.²²¹ This section addresses each of these errors in turn, and proposes an alternative that, while protecting the FDA's mission, would also protect the First Amendment rights of manufacturers as speakers.

A. The Government's Substantial Interest Redefined

Courts considering the constitutionality of the FDA's prohibition on off-label promotion thus far²²² have erred in their conception of the government's substantial interest served by regulating off-label promotion. The root of the FDA's regulatory authority is the FDCA.²²³ In the FDCA, Congress announced the purpose of the agency:

The [Food and Drug] Administration shall—

- (1) Promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner;
- (2) . . . protect the public health by ensuring that . . . (b) human . . . drugs are safe and effective²²⁴

Yet despite the clear Congressional mandate that the FDA promote public health, the FDA's purpose has been distorted or misconceived repeatedly by both the FDA and courts in litigation surrounding the constitutionality of the FDA's regulation of off-label promotion.²²⁵

WLF I recognized that Supreme Court precedent has repeatedly held the protection of the public's health and safety to be a

²²⁰ See *United States v. Caputo*, 288 F. Supp. 2d 912, 922 (N.D. Ill. 2003).

²²¹ See *Caronia*, 576 F. Supp. 2d at 401; see also *infra* Part IV.C.

²²² See generally *Alliance for Natural Health U.S. v. Sebelius*, 714 F. Supp. 2d 48 (D.D.C. 2010); *Caronia*, 576 F. Supp. 2d at 385; *Caputo*, 288 F. Supp. 2d at 912; *WLF I*, 13 F. Supp. 2d 51 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000); Complaint, *Allergan*, *supra* note 46.

²²³ Food, Drug & Cosmetic Act, 21 U.S.C.A. §§ 301–99 (West 2010).

²²⁴ *Id.* §§ 393(b)(1–2) (emphasis added).

²²⁵ See, e.g., *Caronia*, 576 F. Supp. 2d at 398; *Caputo*, 288 F. Supp. 2d at 921; *WLF I*, 13 F. Supp. 2d at 70–71.

substantial government interest, and admonished that “[a]ny claim that the government’s general interest is insufficient under *Central Hudson* is frivolous.”²²⁶ Certainly, that interest is substantial, if not compelling; but the court went further to assess the government’s purported interests.²²⁷ It properly rejected the government’s contention that the FDA could restrict speech out of fear that the information will be misused²²⁸ because “[i]f there is one fixed principle in the commercial speech arena, it is that ‘a State’s paternalistic assumption that the public will use truthful, nonmisleading commercial information unwisely cannot justify a decision to suppress it.’”²²⁹ It accepted, however, the argument that the FDA had a substantial interest in compelling manufacturers to subject uses of a drug to the FDA approval process.²³⁰ *WLF I* noted, apparently with approval, that conditioning a manufacturer’s ability to disseminate any information about a particular use of its drug on FDA approval would “encourage[, if not compel]” the manufacturer to seek approval for off-label uses of its drugs.²³¹ The *Caputo* court adopted the *WLF I* reasoning regarding substantial government interest²³² and held that permitting off-label promotion would “completely undermine the government’s interest in subjecting off-label uses to the FDA’s evaluation process as well as the government’s interest in preserving the integrity of the FDCA’s new drug approval process.”²³³

Caronia adopted the reasoning from *WLF I* and *Caputo*, recognizing “the government’s substantial interest in subjecting off-label uses of a drug . . . to the FDA’s evaluation process.”²³⁴

²²⁶ *WLF I*, 13 F. Supp. 2d at 69.

²²⁷ *See id.* at 69–70.

²²⁸ *Id.*

²²⁹ *Id.* (citing 44 *Liquormart v. Rhode Island*, 517 U.S. 484, 497 (1996)).

²³⁰ *Id.* at 70.

²³¹ *Id.*

²³² *United States v. Caputo*, 288 F. Supp. 2d 912, 921 (N.D. Ill. 2003).

²³³ *Id.*

²³⁴ *United States v. Caronia*, 576 F. Supp. 2d 385, 398 (E.D.N.Y. 2008) (citing, *inter alia*, *WLF I*, 13 F. Supp. 2d at 70–71; *Caputo*, 288 F. Supp. 2d at 921).

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Although it acknowledged the government's substantial interest in ensuring the health and safety of its citizens, identified in *WLF I*,²³⁵ it erred in accepting the FDA's interest in compelling manufacturers to seek additional indications via the FDA approval process as an additional substantial interest.²³⁶ Perhaps even more obviously, its adoption of *Caputo's* holding that the success of the FDCA is a substantial government interest²³⁷ betrays a fundamental misconception of the policies and purposes served by the FDA's approval process.²³⁸ "Preserving the integrity"²³⁹ of a statutory scheme such as the FDCA is no more a substantial government interest than is preserving the integrity of Rhode Island's law forbidding advertisement of retail alcoholic beverages.²⁴⁰ Ensuring the success of a law must be subordinated to constitutional concerns.²⁴¹ Subjecting new uses of drugs to the FDA's approval process and ensuring the rigor of the FDCA are means to an end—namely, promoting the public health and safety—but neither is an end unto itself.²⁴² The substantial—indeed compelling—interest served by the FDA's regulatory scheme is, and should be conceived of as, ensuring public health

²³⁵ See *WLF I*, 13 F. Supp. 2d at 69.

²³⁶ See *Caputo*, 288 F. Supp. 2d at 921; *WLF I*, 13 F. Supp. 2d at 70–71.

²³⁷ *Caputo*, 288 F. Supp. 2d at 921 (citing *Thompson v. Western States Medical Center*, 535 U.S. 357, 369 (2002)).

²³⁸ See Ball, Duffy & Russakoff, *supra* note 88, at 7–9 (implying that courts applying *Western States* have improperly balanced this interest against free speech rights).

²³⁹ *Caputo*, 288 F. Supp. 2d at 921.

²⁴⁰ Compare 44 *Liquormart v. Rhode Island*, 517 U.S. 484, 489–90, 490 n.2 (1996) with Rhode Island Gen. Laws § 3-8-7 (1987).

²⁴¹ See *Marbury v. Madison*, 5 U.S. 137, 177 (1803) ("Certainly all those who have framed written constitutions contemplate them as forming the fundamental and paramount law of the nation, and consequently the theory of every such government must be, that *an act of the legislature, repugnant to the constitution, is void.*" (emphasis added)).

²⁴² Even assuming, *arguendo*, however, that the government may have a substantial interest in subjecting new drug uses to FDA scrutiny, less restrictive means of achieving this goal are available. The proposed disclosure requirement, see *infra* Part IV.C, would advance this goal by incentivizing manufacturers to seek to bolster their promotional claims with the FDA's approval.

and safety: this comports with Congress' intent in forming the FDA,²⁴³ with the history of drug regulation generally,²⁴⁴ and with the FDA's conception of its own mandate.²⁴⁵

B. Medical Marketplace, Meet the Marketplace of Ideas: Off-Label Speech Directly Advances Public Health and Safety

Promotion of public health and safety is best served by the free exchange of truthful, non-misleading information regarding potential drug therapies, regardless of whether a particular use has been approved by the FDA.²⁴⁶ The *WLF I* Court recognized this fact, writing:

the open dissemination of scientific and medical information regarding [off-label] treatments is of great import. The FDA acknowledges that physicians need reliable and up-to-date information concerning off-label

²⁴³ See Food, Drug & Cosmetic Act, 21 U.S.C.A. §§ 393(b)(1)–(2) (West 2010).

²⁴⁴ See generally JAMES T. O'REILLY, FOOD AND DRUG ADMINISTRATION §§ 3.1–3.12 (3d ed. 2005). The precursor to the FDA was the Department of Chemistry. The Pure Food and Drugs Act was passed in 1906, see Pure Food and Drug Act, 34 Stat. 768 (1906), in response to public outcry over the abhorrent conditions in meat-packing facilities. See generally UPTON SINCLAIR, THE JUNGLE (1905). The Act announced as the Department of Chemistry's purpose "preventing the manufacture, sale, or transportation of . . . misbranded . . . or deleterious foods, drugs, medicines, and liquors . . ." Pure Food and Drug Act, 34 Stat. 768 (1906). In 1912, through the Sherley Amendment, the category of misbranding offenses was expanded to include false or fraudulent statements about drugs. 37 Stat. 416 (1911). The Department of Chemistry was reorganized and dissolved in 1927, leading to the formation of the FDA. O'REILLY, *supra*, § 3.3 (3d ed. 2005).

²⁴⁵ *What We Do*, FDA.GOV (last updated Nov. 18, 2010) <http://www.fda.gov/AboutFDA/WhatWeDo/default.htm> ("*protecting the public health* by assuring the safety, efficacy, and security of human . . . drugs" (emphasis added)).

²⁴⁶ See Ball, Duffy & Russakoff, *supra* note 88, at 7 ("[S]urely there is . . . a substantial interest in providing open access to available data about unapproved uses for drugs because it results in more informed and therefore safer medical decision making.").

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uses The need for reliable information is particularly acute in the off-label treatment area because the primary source of information usually available to physicians – the FDA approved label – is absent.²⁴⁷

Under the current regulatory scheme, manufacturers are prohibited from distributing truthful, non-misleading information that is not in the current, FDA-approved labeling.²⁴⁸ This state of affairs is anathema to the promotion of public health and safety repeatedly recognized to be a substantial or even compelling interest: “the FDA’s public protection mandate should lead it . . . to welcome the wide circulation of contemporaneous and accurate scientific data on off-label pros and cons.”²⁴⁹ Indeed, the FDA itself envisions its function with regard to drugs as “protecting the public health by assuring the safety, efficacy, and security of human . . . drugs[;] advancing the public health by helping to speed innovations . . . [;] and by *helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health.*”²⁵⁰ Recently, the FDA appears to have recognized that its prohibition of off-label speech may diminish public health.²⁵¹ The government’s interest is served, not

²⁴⁷ *WLF I*, 13 F. Supp. 2d 51, 56 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000) (emphasis added). *See also id.* at 55 (noting that an inherent contradiction in the FDA’s regulation of off-label promotion is that “what a manufacturer may lawfully claim that a drug does under the statutory and regulatory scheme, and what a physician may prescribe a drug for, do not match”).

²⁴⁸ *See Osborn, supra* note 88, at 328.

²⁴⁹ Smith, *supra* note 43, at 971; *see also Fritch, supra* note 70, at 364 (advocating mandatory disclosure by pharmaceutical manufacturers of all clinical data regarding the drugs they promote).

²⁵⁰ *What We Do*, FDA.gov, *supra* note 245 (emphasis added).

²⁵¹ *See* GOOD REPRINT PRACTICES, *supra* note 16 § III (“[The] FDA does recognize, however, the important public health and policy justification supporting dissemination of truthful and non-misleading medical journal articles and medical or scientific reference publications on [off-label] uses of approved drugs . . . to healthcare professionals and healthcare entities. . . . These off-label uses or treatment regimens may be important and may even constitute a medically recognized standard of care. *Accordingly, the public health may be advanced by healthcare professionals’ receipt of medical [literature] on*

by suppression of off-label information, but by its dissemination.²⁵²

Critics of this position point to the potential for manufacturers to manipulate or mislead physicians by sharing only favorable information regarding their products.²⁵³ This complaint is unfounded for three reasons. First, as noted above, off-label promotion is not inherently misleading.²⁵⁴ Second, even assuming a manufacturer did attempt to mislead physicians, market competition would drive the dissemination of not only favorable information, but also information revealing any risks or inefficacies of the drugs.²⁵⁵ Competing manufacturers, insurance companies, pharmacy benefit managers, and states often “counterdetail” by disseminating information about either the superior efficacy of their own product or the lack of efficacy in their competitors’ drugs.²⁵⁶ Thus, while the manufacturer of drug

unapproved new uses of approved or cleared medical products that are truthful and not misleading.” (emphasis added).

²⁵² See Peter E. Kalb & Paul E. Greenberg, *Legal and Economic Perspectives Concerning US Government Investigations of Alleged Off-Label Promotion by Drug Manufacturers*, 27 PHARMACOECONOMICS 623, 624 (2009) (“[I]t may follow that suppressing untruthful or misleading information advances public health, but there is no reason to believe that suppressing the dissemination of truthful, non-misleading information will have that same effect.”); Byron Stier, *Promotion of Off-Label Use: In Favor of a Regulatory Retreat*, 19 ALB. L. J. SCI. & TECH. 609, 609 (2009) (arguing that “the FDA’s background prohibition on off-label promotion should recede and just go away” in part because the prohibition “is counterproductive because it curtails the dissemination of useful information that doctors need to make informed judgments”).

²⁵³ See Marc J. Scheineson & M. Lynn Sykes, *Major New Initiatives Require Increased Disclosure of Clinical Trial Information*, 60 FOOD & DRUG L.J. 525, 543 (2005) (noting that “there have been a number of allegations of pharmaceutical and device companies selectively disclosing favorable clinical trials and/or failing to disclose unfavorable clinical trial results”). *But see infra* Part IV.C (discussing a potential disclosure solution).

²⁵⁴ See *United States v. Caronia*, 576 F. Supp. 2d 385, 397–98 (E.D.N.Y. 2008); *WLF I*, 13 F. Supp. 2d 51, 65–69 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000). *See also supra* §§ II.C.1–2.

²⁵⁵ *Cf. Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council*, 425 U.S. 748, 772 n.24 (1976) (noting the hardness of commercial speech).

²⁵⁶ See, e.g., *IMS Health, Inc. v. Sorrell*, 630 F.3d 263, 280 (2d Cir. 2010) *cert granted* 131 S.Ct. 857 (2011) (indicating Vermont has a “counter-speech”

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X may trumpet to physicians a new study showing a promising new use for drug X, the manufacturer of competing drug Y has an economic incentive to inform those same physicians of five studies showing that drug X is inefficacious for that use. The result is the dissemination of a broad range of scientific information, leading to a richer marketplace of ideas and a better-informed medical community.

Third, the paternalistic view that the government may suppress speech where the recipients of the speech may misuse the information provided has been repeatedly rejected in the context of off-label promotion,²⁵⁷ and beyond.²⁵⁸ The Supreme Court has noted that “people will perceive their own best interests if only they are well enough informed, and . . . the best means to that end is to open the channels of communication rather than to close them.”²⁵⁹ Furthermore, the Second Circuit recently struck down a paternalistic Vermont statute that limited the availability to doctors of information regarding medications.²⁶⁰ Vermont prohibited manufacturers from using information about physicians’ prescribing habits, compiled and sold by data mining companies, in order to tailor promotional speech to each physician’s need.²⁶¹

program in place to disseminate information to physicians).

²⁵⁷ See *Caronia*, 576 F. Supp. 2d at 398 (citing 44 *Liquormart v. Rhode Island*, 517 U.S. 484, 497 (1996)); *WLF I*, 13 F. Supp. 2d at 69–70 (“To the extent that the FDA is endeavoring to keep information from physicians out of concern that they will misuse that information, the regulation is wholly and completely unsupported.”).

²⁵⁸ See *Citizens United v. F.E.C.*, 130 S. Ct. 876, 896 (2010) (holding that the government may not “select what . . . speech is safe for public consumption by applying an ambiguous test”); 44 *Liquormart*, 517 U.S. at 497; *Cent. Hudson Gas & Elec. Co. v. Pub. Serv. Comm’n N.Y.*, 447 U.S. 557, 562 (1980) (“[W]e have rejected the ‘highly paternalistic’ view that government has complete power to suppress or regulate commercial speech.”); *Va. State Bd. of Pharmacy*, 425 U.S. at 770.

²⁵⁹ *Va. State Bd. of Pharmacy*, 425 U.S. at 770.

²⁶⁰ *IMS Health*, 630 F.3d at 267 (“We conclude that because [the challenged statute] is a commercial speech restriction that does not advance the substantial state interests asserted by Vermont, and is not narrowly tailored to advance those interests, the statute cannot survive intermediate scrutiny under *Central Hudson*.”).

²⁶¹ See VT. STAT. ANN. tit. 18 §§ 4631(a) & (d) (2010).

The Vermont legislature gave several justifications for this statute, including: (1) the aims of manufacturers in marketing their drugs “often . . . conflict with the goals of the state”;²⁶² (2) the “marketplace for ideas on medicine safety and effectiveness is frequently one-sided” resulting in prescribing based upon “incomplete and biased information”;²⁶³ and (3) “[p]ublic health is ill served by the massive imbalance in information presented to doctors.”²⁶⁴ Finding that the Vermont legislature “inten[ded] to interfere with the marketplace of ideas to promote the interests of the state,”²⁶⁵ the Second Circuit struck down Vermont’s statute, and noted that, even if Vermont succeeded in manipulating physicians’ prescribing habits, “the Supreme Court reminds us that ‘[i]t is precisely this kind of choice, between the dangers of suppressing information, and the dangers of its misuse if it is freely available, that the First Amendment makes for us.’”²⁶⁶

Physicians’ prescribing decisions, and therefore the public health, will be improved if physicians are well-informed about potential off-label uses. When prescribing medications, physicians need to know whether a medication is a safe and effective treatment: the research of other physicians, scientists, and academics constitutes an essential source of this information.²⁶⁷ Manufacturers are in a unique position as the most efficient aggregators of information about their products, to disseminate such information to physicians.²⁶⁸ The FDA’s policy of absolute suppression of manufacturer dissemination of this information

²⁶² Vt. Act No. 80 § 1(3) (2007).

²⁶³ *Id.* § 1(4).

²⁶⁴ *Id.* § 1(6).

²⁶⁵ *IMS Health*, 630 F.3d at 270 (citing Vt. Act No. 80 § 1).

²⁶⁶ *Id.* at 270 (citing *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council*, 425 U.S. 748, 770 (1976)).

²⁶⁷ *WLF I*, 13 F. Supp. 2d 51, 63 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000).

²⁶⁸ See Stier, *supra* note 252, at 610–11; Smith, *supra* note 43, at 971–72. See also *Va. State Bd. of Pharmacy*, 425 U.S. at 772 n.24 (“[O]rdinarily the advertiser seeks to disseminate information about a specific product or service that he himself provides and presumably knows more about than anyone else.” (emphasis added)).

frustrates, rather than serves, the interest of enhancing and protecting public health.

*C. Less Speech-Restrictive Means of Enhancing Public Health:
Citizens United's Approval of Disclosure and
Disclaimer and the Benefit of Sophisticated Consumers*

Given the clarification of the government's substantial interest in regulating off-label promotion—enhancing public health and safety²⁶⁹—and the failing of a complete ban on off-label speech to achieve that interest,²⁷⁰ it follows that the current regulatory scheme is more restrictive than necessary. Despite *Caronia*'s inability to identify any less speech-restrictive means,²⁷¹ such means do exist and have been proposed.²⁷² The most promising—and least speech-restrictive—means of regulating off-label promotion while remaining respectful of the speakers' constitutional rights comes from what is, at first blush, an unlikely source.

Despite the deep divide between political and commercial speech, much of the reasoning in *Citizens United* applies just as well to heavily-regulated commercial speech.²⁷³ The parallel infirmities of the regulatory schemes at issue in *Citizens United* and *Caronia* suggest that the less speech-restrictive means

²⁶⁹ See *supra* Part IV.A.

²⁷⁰ See *supra* Part IV.B.

²⁷¹ See *United States v. Caronia*, 576 F. Supp. 2d 385, 401–02 (E.D.N.Y. 2008); see also Ball, Duffy & Russakoff, *supra* note 88, at 1.

²⁷² Blackwell & Beck, *supra* note 88, at 456 (“Other alternatives include: 1) permitting off-label promotion to physicians but not consumers; 2) permitting promotion through any means other than direct to consumer advertising; 3) permitting speech promoting off-label uses except on product labels; and 4) simply clarifying the boundaries between dissemination of off-label information that is considered promotional and, thus, prohibited and dissemination that is considered nonpromotional and, thus, permitted.”); see also Ball, Duffy & Russakoff, *supra* note 88, at 1 (proposing alternative means of encouraging manufacturers to seek additional indications for their medication while respecting free speech rights).

²⁷³ See *supra* Part III.B.

proposed in *Citizens United*²⁷⁴ would be equally applicable in the off-label promotion context. In striking down section 441's ban on corporate independent expenditures, *Citizens United* upheld the requirement that corporations disclose their sponsorship of the messages.²⁷⁵ Relying on precedent that found the government's interest in the prevention of real or apparent corruption inadequate to justify a ban on independent expenditures,²⁷⁶ the Court held that disclosure and disclaimer is a "less restrictive alternative to more comprehensive regulations of speech"²⁷⁷ that avoided the constitutional infirmities of an outright ban.

Although First Amendment jurisprudence traditionally frowns on compelled speech,²⁷⁸ compelled disclosures in commercial speech are favored over the alternative here: complete suppression of a particular type of commercial speech.²⁷⁹ Thus, if a required disclosure would be a constitutional means of "permit[ing] citizens and shareholders to react to the [political] speech of corporate entities in a proper way,"²⁸⁰ certainly, it would be constitutional in regard to commercial speech, where compelled speech is already less problematic,²⁸¹ in order to facilitate the

²⁷⁴ See *Citizens United v. F.E.C.*, 130 S. Ct. 876, 915 (2010).

²⁷⁵ Compare *id.* at 913–14 with Bipartisan Campaign Reform Act, 2 U.S.C.A. §§ 441d(a)(3), (d)(2) (West 2010).

²⁷⁶ *Citizens United*, 130 S. Ct. at 901–02 (citing *Buckley v. Valeo*, 424 U.S. 1, 26 (1976)).

²⁷⁷ *Id.* at 915.

²⁷⁸ See, e.g., *West Virginia Bd. of Ed. v. Barnette*, 319 U.S. 624, 634 (1943) (refusing to sustain a statute mandating a compulsory flag salute in public schools); *United States v. United Foods, Inc.*, 533 U.S. 405, 410 (2001) ("Just as the First Amendment may prevent the government from prohibiting speech, the Amendment may prevent the government from compelling individuals to express certain views.").

²⁷⁹ See *WLF I*, 13 F. Supp. 2d 51, 73 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000) (finding "the restrictions in the Guidance Documents are considerably more extensive than necessary to further the substantial government interest in encouraging manufacturers to get new uses on-label"); *Bates v. State Bar Ass'n of Arizona*, 433 U.S. 350, 375 (1970) (noting that the "preferred remedy is more disclosure, rather than less").

²⁸⁰ See *Citizens United*, 130 S. Ct. at 915.

²⁸¹ See *WLF I*, 13 F. Supp. 2d at 70.

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dissemination of accurate information regarding the off-label use of drugs.

Given the fact that a physician is the targeted recipient of the off-label speech,²⁸² disclosure would likely be an even more effective regulatory strategy in the off-label context than in the political speech context. Physicians are sophisticated consumers of speech regarding off-label drug uses: they are well aware of the implications for safety and efficacy inherent in a prescription drug's off-label status.²⁸³ A disclosure to physicians that the advocated use (1) is being advanced by a speaker with a commercial interest in the product, and (2) has not been approved as safe and effective by the FDA, would signal the need for a discerning approach to the information provided and caution in the use of the drug for that purpose.²⁸⁴

Concerns have been raised about the potential for a manufacturer engaging in off-label promotion to skew the information provided to physicians by sharing only favorable information about a drug's efficacy for an off-label use, while downplaying or omitting information that suggests inefficacy.²⁸⁵ Consistent with the First Amendment, the FDA could require manufacturers to disseminate a bibliography, complete with abstracts, of all scientific literature, favorable and unfavorable, discussing the off-label use which the manufacturer proposes.²⁸⁶ In

²⁸² See *id.* at 63.

²⁸³ See *id.* (noting that “despite the FDA’s occasional statements in its briefs to the contrary, physicians are a highly educated, professionally-trained and sophisticated audience”).

²⁸⁴ See *id.* at 73 (Faced with such a disclosure, “[a] physician would be immediately alerted to the fact that the ‘substantial evidence standard’ had not been satisfied, and would evaluate the communicated message accordingly.”).

²⁸⁵ See Fritch, *supra* note 70, 357 (“For any given prescription drug therapy, there may be a variety of positive and negative studies available, yet drug manufacturers are motivated only to promote studies that reflect positively on their drug.”).

²⁸⁶ See, e.g., *WLF I*, 13 F. Supp. 2d at 73. Here, although compelled speech is often suspect under First Amendment jurisprudence, it is the lesser of two evils. See *Bates v. State Bar Ass’n of Arizona*, 433 U.S. 350, 375 (1970). For example, under such a regime, Mr. Caronia could have discussed with the physician the use of Xyrem in fibromyalgia patients, one of the off-label uses he

fact, under the FDA's most recent guidance for the dissemination of scientific literature that discusses off-label uses of medications, similar requirements exist.²⁸⁷ Given the existence of such a requirement, concerns about misleading dissemination of off-label information are unfounded.

Critics of a disclosure-based approach to regulating off-label promotion may be concerned that allowing off-label promotion, even with disclosure, may circumvent the FDA's approval process;²⁸⁸ however ample opportunities to implement incentives to seek on-label status for drugs remain available.²⁸⁹ The government would be free to, *inter alia*

preempt product liability cases for products that receive FDA approval, but preserve product liability theories against uses which have not received FDA approval[;] . . . provide several economic incentives to encourage companies to seek FDA approval for new uses[;] . . . [or] establish a streamlined approval process for an already-approved drugs' additional widespread uses.²⁹⁰

was originally accused of promoting. If he chose to do so, he would be required to provide the physician with a bibliography containing the peer-reviewed, medical journal articles discussing this use for Xyrem. *See* PUBMED, <http://www.pubmed.gov> (last visited Apr. 8, 2010) (search for "sodium oxybate fibromyalgia").

²⁸⁷ *See* GOOD REPRINT PRACTICES, *supra* note 16 § 4.B (mandating that manufacturers must disseminate "a comprehensive bibliography of publications discussing adequate and well-controlled clinical studies published in medical journals or medical or scientific texts about the use of the drug" and "a representative publication, when such information exists, that reaches contrary or different conclusions regarding the unapproved use").

²⁸⁸ *See, e.g.,* United States v. Caputo, 288 F. Supp. 2d 912, 921 (N.D. Ill. 2003) ("Manufacturers, knowing that they could promote off-label uses, would have an incentive only to seek FDA approval for uses that would be approved easily and inexpensively. Thus, the Court holds that subjecting off-label uses to the FDA's evaluation process is a substantial governmental interest.") *But see supra*, Part IV.A (noting paternalistic fears of misuse of speech does not justify suppression of the speech).

²⁸⁹ Blackwell & Beck, *supra* note 88, at 456 (listing additional, less speech restrictive safeguards against circumvention of the approval process).

²⁹⁰ Ball, Duffy & Russakoff, *supra* note 88, at 1. *See also* Blackwell & Beck, *supra* note 88, at 456.

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Additionally, the very fact that a particular use is off-label may give some physicians pause. Even under a disclosure regime, there is a clear economic incentive to “get off-label treatments on-label,”²⁹¹ obviating the perceived need for the FDA’s current oppressive regulatory scheme.

V. CONCLUSION

Caronia presents a concrete example of the ramifications for free speech inherent in the FDA’s current regulatory regime. Fortunately, the constitutional infirmities of the FDA’s scheme can be remedied by a straightforward application of First Amendment law, including, in particular, the recent decision in *Citizens United*. The complexity of the FDA’s scheme, like the FEC’s in *Citizens United*, is so abstruse that it essentially functions as a prior restraint. This *de facto* prior restraint is indefensible, however, upon a careful examination of the purpose and fit of the FDA’s stranglehold on off-label speech. This stranglehold may ensure the sanctity of the FDA’s regulatory scheme, but this, in itself, is not a substantial governmental interest: the FDA’s only substantial interest in regulating off-label promotion is the promotion of public health and safety. Dissemination, not suppression, of scientific information regarding off-label uses of drugs serves this interest. To the extent that concern may linger as to a potential conflict of interest between the promotion of public health and the manufacturer’s commercial interests, the Supreme Court, in *Citizens United*, has approved of a less restrictive means of policing this conflict:²⁹² candid disclosure of the manufacturer’s financial interest in the off-label speech should replace the current prohibition.²⁹³ An appeal of *Caronia* is currently pending:²⁹⁴ therefore the Second Circuit, and potentially the Supreme Court,

²⁹¹ *United States v. Caronia*, 576 F. Supp. 2d 385, 398 (E.D.N.Y. 2008).

²⁹² *Citizens United v. F.E.C.*, 130 S. Ct. 876, 915 (2010).

²⁹³ See *WLF I*, 13 F. Supp. 2d 51, 73 (D.D.C. 1998), *vacated sub nom. WLF III*, 202 F.3d 331 (D.C. Cir. 2000).

²⁹⁴ See Unofficial Oral Argument Transcript, *United States v. Caronia*, No. 09 Cr. 5006 (2d Cir. Dec. 2, 2010) (on file with author); *Caronia* Brief, *supra* note 1.

will soon have the opportunity to correct the constitutional deprivations currently worked by the FDA and to extend protection to a subset of commercial speech essential to the public health.