

THE FUTURE OF OFF-LABEL MARKETING REGULATIONS IN THE POST-SORRELL ERA

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I. INTRODUCTION

With expanding constitutional protection of corporate speech rights, the Supreme Court is poised to consider the next big challenge: off-label marketing restrictions enforced by the federal government. The First Amendment challenge to the Food and Drug Administration's (FDA) off-label marketing guidelines has been brewing for over a decade; with the recent Supreme Court decision in *Sorrell v. IMS Health, Inc.*, it seems likely that the challenge will work its way back on to the Federal Court docket.¹

Off-label is the practice of using prescription drugs for purposes that have not been specifically approved by the FDA.² It is estimated that twenty percent of prescriptions in America are for off-label uses.³ The practice is most commonly seen in pediatrics, psychiatry, and oncology.⁴ For diseases affecting a very small subset of the population, or for high-risk illnesses, off-label prescriptions are often a patient's only available treatment option.⁵ While physicians are free to prescribe drugs for any off-label indication that meets the appropriate medical standard of care, drug companies are prohibited from marketing products for any purpose that is not specifically

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¹ *Sorrell v. IMS Health, Inc.*, 131 S. Ct. 2653 (2011).

² Randall S. Stafford, M.D., Ph.D., *Regulating Off-label Drug Use—Rethinking the Role of the FDA*, 358 NEW ENGLAND J. OF MED. 1427, 1428 (Apr. 3, 2008).

³ Radley, Finkelstein, & Stafford, *Off-Label Prescribing Among Office-Based Physicians*, 166 ARCHIVES OF INTERNAL MED. 1021–26 (2006).

⁴ Rebecca Dresser & Joel Frader, *Off-Label Prescribing: A Call for Heightened Professional and Government Oversight*, 37 J.L. MED. & ETHICS 476, 476 (2009).

⁵ Gregory Gentry, *Criminalizing Knowledge: The Perverse Implications of the Intended Use Regulations for Off-Label Promotion Prosecutions*, 64 FOOD & DRUG L.J. 441, 442 (2009).

included on the product labeling (i.e. off-label indications).⁶

Drug manufacturers have a vested interest in the regulations governing the prescription and marketing of off-label drugs. They invest hundreds of millions of dollars to push potential medications through the cumbersome FDA-approval process; the estimated average cost to bring a new drug to market in the United States is just under \$900 million.⁷ This lofty capital investment gives pharmaceutical manufacturers significant incentive to see their brand name drug prescribed widely and often.

The bottom-line leaves drug manufacturers hoping that their drug is prescribed for a variety of diseases. Unfortunately, when pushing a drug through the FDA approval process, companies rarely seek approval to treat multiple illnesses.⁸ More commonly, a company will seek approval for a few targeted applications and hope that physicians prescribe the drug for other reasons as well.⁹ Physicians are free to prescribe medications to patients for reasons other than those listed on the manufacturer's product insert.¹⁰

While physicians are free to prescribe FDA-approved medications for any reason they deem medically appropriate, drug manufacturers are prohibited from marketing their products for off-label indications.¹¹ The consequences are often catastrophic for manufacturers guilty of off-label marketing violations, including fines in the tens or hundreds of millions of dollars.¹² In 2009, for example, Pfizer paid a fine of \$2.3 billion to the FDA for off-label marketing of their drug Bextra.¹³ Such damaging fines give pharmaceutical

⁶ Stafford, *supra* note 2, at 1427.

⁷ *Greater Access to Generic Drugs: New FDA Initiatives to Improve the Drug Review Process and Reduce Legal Loopholes*, U.S. FOOD AND DRUG ADMIN. (Jan. 2006), <http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143545.htm> ("According to the Boston-based Tufts Center for the Study of Drug Development, the cost to develop a new drug averages \$897 million.").

⁸ See Dresser, *supra* note 4, at 476.

⁹ *Id.*

¹⁰ *Id.*

¹¹ John E. Osbourne, *Can I Tell the Truth: A Comparative Perspective on Regulating Off-Label Scientific and Medical Information*, 10 YALE J. HEALTH POL'Y L. & ETHICS 299, 301, 303 (2010); see also 21 U.S.C. §§ 331(a), (b), (d) (2012).

¹² Antonia Guiliani, *Statistics for Off-Label Marketing Settlements Involving Prescription Drugs*, KELLEY DRYE WARREN LLP (Mar. 2, 2011), <http://www.fcaalert.com/2011/03/articles/settlements-1/statistics-for-offlabel-marketing-settlements-involving-prescription-drugs/>.

¹³ Thomas Burton, *The Free Speech Pill: Drug Firms See Opening to Push for End to Off-Label Marketing Ban*, WALL ST. J., Nov. 3, 2011, available at <http://online.wsj.com/article/SB10001424052970203707504577012382844711146.html>.

companies considerable incentive to challenge off-label marketing regulations, leaving some scholars to speculate that pharmaceutical companies have begun challenging violations on First Amendment grounds.¹⁴

Off-label marketing regulations have long been criticized for their imprecision and unpredictable standards.¹⁵ The government prosecutes off-label marketing violations in two manners: through the Food and Drug Cosmetic Act (FDCA) and the Federal False Claims Act (FCA).¹⁶ The FDCA sets forth the regulations for manufacturing and branding pharmaceuticals in the United States.¹⁷ The misbranding provision allows prosecutors to punish companies that make assertions inconsistent with their products' approved drug labels.¹⁸ The FDA has offered little guidance to define the scope of this provision, leaving drug manufacturers eager to see its demise.¹⁹

Recently, pharmaceutical companies were given new ammunition to fight the federal guidelines with the Supreme Court's decision in *Sorrell*.²⁰ The Court held that the practice of data mining, used by pharmaceutical companies to create more effective detailing practices,²¹ constitutes protected speech under the First Amendment.²² The Court determined that Vermont's law, which proscribed pharmacies from selling information regarding physician prescription patterns, created both speaker-based and content-based speech restrictions.²³ The majority in *Sorrell* held that the law was unconstitutionally burdensome on the company's free speech rights.²⁴ The Court found that the State's justifications for the law were substantial but that the means to achieve those ends were not

¹⁴ *Id.* See also Kevin Outterson, *The Last Drug Company Settlement for Off-Label Promotion*, THE INCIDENTAL ECONOMIST (Nov. 3, 2011), <http://theincidentaleconomist.com/wordpress/the-last-drug-company-settlement-for-off-label-promotion/>.

¹⁵ Bennett, Kalb, McPhee & Klasmeier, *Citizen Petition to the FDA* (Jul. 5, 2011), available at <http://www.fdalawyersblog.com/allergan0900006480eba5de%5B1%5D.pdf>.

¹⁶ 31 U.S.C. § 3729 (2006); 21 U.S.C. §§ 301–399 (2006).

¹⁷ 21 U.S.C. §§ 301–399 (2006).

¹⁸ 21 U.S.C. § 352(a).

¹⁹ See Osbourne, *supra* note 11, at 316–17.

²⁰ See *Sorrell v. IMS Health, Inc.*, 131 S. Ct. 2653 (2011).

²¹ “Detailing” is the practice of marketing prescription drugs to healthcare professionals with the intent to induce the healthcare professionals to prescribe a certain prescription drug more readily. *Sorrell*, 131 S. Ct. at 2659.

²² *Id.*

²³ *Id.*

²⁴ *Id.* at 2672.

narrowly tailored.²⁵

The primary purpose of this Comment is to discuss the likelihood of success for the imminent judicial challenge to off-label marketing regulations following *Sorrell*. *Sorrell's* application of strict scrutiny within the context of a corporate free speech action is novel, while the decision's dicta are also powerfully predictive. In future challenges, drug companies will be required to counter any state's assertions that the off-label marketing restrictions are narrowly tailored to achieve a substantial State interest. Doing so will require pharmaceutical companies to persuade the Court that there are reasonable, less restrictive alternatives to the current regulations.

Part II of this Comment begins with a discussion of the history and practice of off-label marketing, as well as the federal regulations overseeing the practice. That section addresses the almost dizzying connection of federal statutes and regulations that the government uses to justify prosecution of off-label marketing. Next, Part III analyzes the Supreme Court decision in *Sorrell*, addressing the relevant First Amendment issues, applicable legal doctrines, and future implications of the case. In Part IV, this Comment addresses additional significant cases that have previously been decided by courts on the off-label marketing issue. Included in the analysis is the Second Circuit Court of Appeals decision in *United States v. Caronia*. Part V confronts how the Court might handle a First Amendment challenge to off-label marketing in the future. Part VI includes a detailed analysis of a quota system as an alternative, and how such a system may or may not be a practical alternative to the current regulatory mechanism. Ultimately, this Comment predicts that the Court will deem the current regulatory scheme unconstitutional, as the proposed alternative quota system is a potential alternative to achieving the government interest.

II. CURRENT STATE OF OFF-LABEL REGULATIONS

A. Drug Approval and Labeling Regulations and Interpretation

Off-label marketing occurs when a pharmaceutical manufacturer endorses a drug for uses that have not passed FDA approval.²⁶ Drugs are approved for a narrow set of conditions; they are not approved for universal use.²⁷ For example, when a drug has been proven safe

²⁵ *Id.*

²⁶ Stafford, *supra* note 2, at 1021.

²⁷ *Cf.* 21 U.S.C. § 355(d)(1) (2006) (noting that an application for a new drug

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and effective in clinical trials to treat cardiac arrhythmia, the FDA might grant approval of the drug, but only for the purpose of treating cardiac arrhythmia. The drug's labeling and specific use will not include information about its efficacy for other disorders.²⁸

When a drug manufacturer proposes a new drug for the treatment of a given disorder, it must follow express FDA regulations.²⁹ The process includes extensive clinical trials.³⁰ These trials enable the manufacturer to demonstrate that the proposed drug is safe and effective for each of its intended uses.³¹ Following these tests, the manufacturer must show that the drug performed safely and effectively in well-controlled clinical trials conducted by qualified scientific experts.³² Unless the drug's labeling represents the conclusions of these studies accurately, the drug will be considered mislabeled.³³

Different documents define the term "labeling" differently. "Labeling" under the FDCA is defined narrowly; it includes all tangible materials that accompany a drug.³⁴ The FDA guidelines, however, define "labeling" more broadly; the FDA includes practically any materials or information that the manufacturer or its employees might produce —whether accompanying the drug or not.³⁵ This casts a significantly broader net and has pervasive implications in terms of the Justice Department's ability to prosecute off-label marketing actions.³⁶

will be denied if it does not "include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof").

²⁸ Cf. 21 U.S.C. § 352(a) (a product label "shall not be considered to be false or misleading under this paragraph if the health care economic information directly relates to an indication approved under section 355 of this title or under section 262(a) of title 42 for such drug and is based on competent and reliable scientific evidence").

²⁹ See 21 U.S.C. § 355 (2006).

³⁰ 21 U.S.C. § 355(o) (3).

³¹ *Id.*

³² See 21 U.S.C. § 355(d) (2012). ("If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.").

³³ 21 U.S.C. § 352(a) (2012).

³⁴ 21 U.S.C. § 321(m), (p) (2012).

³⁵ Osbourne, *supra* note 11, at 308 (citing 21 C.F.R § 202.1 (2009)).

³⁶ *Id.* (citing 62 Fed. Reg. 64074, 64085 (Dec. 3, 1997)).

B. *Prosecution for Violations of Off-Label Marketing Regulations Through the FDCA and FCA*

i. Violations under the FDCA for Introducing a Misbranded Drug into Interstate Commerce

The Justice Department currently enforces off-label marketing violations through the Food Drug and Cosmetic Act's Labeling and Misbranding provisions. It might come as a surprise that there is not in fact any express proscription of off-label marketing of pharmaceuticals in the FDCA.³⁷ Rather, the federal government enforces the policy through a number of other means, including misbranding and mislabeling provisions.³⁸ As noted above, the FDCA sets forth the labeling rules that manufacturers must abide by in order to develop and distribute pharmaceuticals in the United States.³⁹

Enforcement decisions are based on a set of guidelines established by the FDA in accordance with its interpretation of the FDCA.⁴⁰ Once a drug completes the extensive FDA approval process, the manufacturer's "labeling" must then expressly specify all "intended uses" for which it has been approved.⁴¹ Claims that the company makes regarding efficacy for any type of treatment will qualify as "intended uses" of the drug.⁴² The FDA regulations require that all "intended uses," and associated "adequate instructions for use," be found on the product label.⁴³ According to John Osbourne, "intended use" includes "all uses objectively intended by the drug manufacturer based upon statements made in labeling, advertisements, or in written or oral statements by company representatives."⁴⁴ As such, when a company makes an assertion about its drug, it is making a statement about the drug's "intended use."⁴⁵ If that "intended use," or associated "adequate instructions for

³⁷ See 21 U.S.C. § 352 ("A drug or device shall be deemed to be misbranded . . . [i]f its labeling is false or misleading in any particular. . . information . . . [but it] shall not be considered false or misleading if . . . information directly relates to an indication approved under section 355 or under section 262(a) of title 42 for such drug and is based on competent and reliable scientific evidence.").

³⁸ Osbourne, *supra* note 11, at 308.

³⁹ See 21 U.S.C. § 352(a) (2012); *see also*, 21 C.F.R. § 201.1–201.58.

⁴⁰ *See id.*

⁴¹ 21 U.S.C. §§ 321(p), 355(a), (b), (j) (2012).

⁴² *Id.*

⁴³ *Id.*

⁴⁴ Osbourne, *supra* note 11, at 309 (citing 21 C.F.R. § 201.128 (2009)).

⁴⁵ Osbourne, *supra* note 11, at 309–10.

use,” are not found on the product’s label, the FDA determines that the manufacturer misbranded the drug.⁴⁶ The FDCA makes it a crime for a company to distribute, or introduce, misbranded drugs into the stream of interstate commerce.⁴⁷

Recently, the Second Circuit Court of Appeals determined that the FDA’s enforcement of off-label marketing under the FDCA, in Caronia’s instance, treats making truthful assertions regarding off-label indications as an act of misbranding itself.⁴⁸ The government’s enforcement of the FDCA treats off-label marketing assertions as more than evincing intent to perform a future act of misbranding.⁴⁹ That is, when a detailer approaches a doctor and makes a valid and truthful claim about the efficacy of Drug X for treating non-approved Indication Y, his act of making this assertion is an instance of misbranding under the government’s interpretation. In this sense, the truthful speech is criminalized.⁵⁰ As addressed below, under the First Amendment the government will likely be prohibited from restricting truthful non-misleading speech in this manner.⁵¹

ii. Violations under the False Claims Act

Alternatively, companies can be held liable under the federal False Claims Act.⁵² A person violates the FCA when he or she knowingly submits or causes to be submitted a false or fraudulent claim for payment or approval.⁵³ Generally, Medicare and Medicaid Services (CMS) will only authorize payments for outpatient drugs if the drug is determined to be “safe and effective.”⁵⁴ Drugs are considered “safe and effective” if they are used for a “medically accepted indication.”⁵⁵ A “medically accepted indication” is one that has been approved by the FDA, included in one of several specified compendia, or is supported by sufficient citations in approved

⁴⁶ *Id.* at 310.

⁴⁷ *See* 21 U.S.C. § 352 (2012).

⁴⁸ *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012).

⁴⁹ *See* Hyman, Phelps & McNamara PC, *A Deep Dive into the Second Circuit’s Caronia Decision, Potential Next Steps, and Potential Enforcement Fallout*, FDA LAW BLOG (Dec. 12, 2012), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2012/12/a-deep-dive-into-the-second-circuits-caronia-decision-potential-next-steps-and-potential-enforcement.html.

⁵⁰ *Id.*

⁵¹ *Id.*

⁵² Osbourne, *supra* note 11, at 310 (citing 31 U.S.C. § 3729 (2006)).

⁵³ 31 U.S.C. § 3729(a)(1)(A) (2012).

⁵⁴ 42 U.S.C. § 1396r-8(k)(2)(A)(i) (2012).

⁵⁵ 42 U.S.C. § 1396r-8(d)(1)(B)(i) (2012).

medical literature.⁵⁶ Submission of a reimbursement claim for an off-label prescription that is not eligible for reimbursement is likely to trigger the FCA.

A manufacturer, or its agent, will be liable under the FCA for making a statement—irrespective of its truth—about the drug, when that statement causes the off-label prescription of a drug that is to be paid for by Medicare or Medicaid.⁵⁷ For example, suppose a pharmaceutical salesman enters a doctor's office and tells the physician "Drug X is useful for treatment of Indication Y." Drug X, however, is only approved for the treatment of Indication Z. Further suppose that the physician then writes a prescription for Drug X to her patient for treatment of Indication Y. The submission of said prescription for payment by Medicare or Medicaid would trigger the FCA.⁵⁸

Surprisingly, it is possible to trigger the FCA without ever making an untruthful, inaccurate, or dishonest representation.⁵⁹ The truthful speech of a detailer that ultimately leads to a patient submitting a claim of reimbursement for an off-label prescription can form the basis of prosecution under the FCA by the government.⁶⁰ What creates the violation—whether it is the submission for reimbursement or the speech—can have a potentially significant impact on future First Amendment challenges to prosecution of off-label marketing restrictions under the FCA.

iii. Implications of Prosecution under FDCA and FCA

The current laws have important implications for the manufacturing and marketing of prescription drugs. First, pharmaceutical companies are significantly restricted in what they can say about their products, truthful or not. As noted above, the regulations do not focus on the truthfulness of marketing statements.⁶¹ Second, the regulations encourage pharmaceutical companies to seek amended secondary approval for additional "intended uses."⁶² This process requires pharmaceutical companies to reenter the FDA drug approval process to receive FDA approval for

⁵⁶ 42 U.S.C. § 1396r-8(k)(6) (2012).

⁵⁷ *Id.* at 310.

⁵⁸ *Cf. Osbourne, supra* note 11, at 329–30.

⁵⁹ *Id.* at 331–32.

⁶⁰ *Id.*

⁶¹ *See supra* Part II.B.ii.

⁶² *See supra* Part II.A.

the additional uses of the medication.⁶³ This allows the manufacturer to change the product label to include additional indications. Once the label is changed, the manufacturer may legally market its product for that purpose, without facing liability under the FDCA and FCA.⁶⁴ Maintaining this requirement ensures that the FDA has reviewed the new uses and observed their safety and efficacy.

Good Reprint guidelines can inhibit manufacturers from distributing certain types of materials and how they must be distributed.⁶⁵ This is contrary to physicians' freedom to conduct, discuss, and distribute information related to off label uses, provided they use appropriate medical diligence.⁶⁶ Additionally, manufacturer financial contributions they might have provided to the reprinted peer reviewed research must be disclosed.⁶⁷

The FDA, however, has established certain safe-harbors that allow for manufacturers to distribute and reprint such information.⁶⁸ For example, if a drug company wants to educate doctors about the benefits of its drug for an off-label use, it is not permitted to

⁶³ See 21 U.S.C. § 321(p)(1) (2012) (“Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof.”); see also 21 U.S.C.A. § 355(a) (West 2012) (“No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application”); Dresser, *supra* note 4, at 477–78.

⁶⁴ See 21 U.S.C.A. § 352(a) (West 2012); see also 21 C.F.R. §§ 201.100(d)(1) (2006).

⁶⁵ *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*, FOOD AND DRUG ADMIN., http://www.fda.gov/regulatory_information/guidances/ucm125126.htm (last visited Apr. 10, 2013) (clarifying the existing safe harbors and violations for pharmaceutical manufacturers that wish to distribute information to physicians and other third parties about effective off label uses of their products). Manufacturers are, however, permitted to disseminate reprints of peer reviewed journal articles that result from research the manufacturer funds, provided they disclose the financial relationship. See *Id.*

⁶⁶ See generally, Randall S. Stafford, M.D., Ph.D., *Regulating Off-label Drug Use—Rethinking the Role of the FDA*, 358 NEW ENGLAND J. OF MED. 1427, 1428 (Apr. 3, 2008).

⁶⁷ See generally, *id.*

⁶⁸ *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*, FOOD AND DRUG ADMIN., http://www.fda.gov/regulatory_information/guidances/ucm125126.htm (last visited Apr. 10, 2013) (“safe harbor” exists “for a manufacturer that complies with [the applicable statutes and regulations] before and while disseminating journal articles and reference publications about ‘unapproved new uses’ of approved or cleared products”).

unilaterally finance the research.⁶⁹ In order to distribute any documents relating to the off-label use of a product, the independently produced publication should be peer reviewed, published by an organization with an expert editorial board, and should not be financed in whole or in part by the manufacturer.⁷⁰ Only then can the drug manufacturer distribute the information, and even still the FDA provides strict guidelines.⁷¹ Furthermore, the information must be an unabridged reprint, free of markings or highlighting, accompanied by a bibliography of similar works, disseminated with contrary data if available, and distributed separately from any information that is promotional in nature.⁷²

Both of these mechanisms—the FDCA and the FCA—give the Justice Department sufficient firepower to prosecute off-label marketing violations. The penalties associated with such prosecutions are severe, in some cases exceeding one billion dollars.⁷³ These large fines give pharmaceutical companies sufficient incentive to challenge the current regulations. It is more than likely that in the near future we will see new constitutional challenges to the off-label marketing regulations. Further, this future challenge is likely to rely heavily on the recent Supreme Court decision in *Sorrell*.

⁶⁹ *Id.* (“A scientific or medical reference publication that is distributed should not be . . . edited or significantly influenced by a drug or device manufacturer or any individuals having a financial relationship with the manufacturer.”).

⁷⁰ *Id.* (“A scientific or medical journal article that is distributed should: be published by an organization that has an editorial board that uses experts who have demonstrated expertise in the subject of the article under review by the organization and who are independent of the organization to review and objectively select, reject, or provide comments about proposed articles.”).

⁷¹ *Id.* (“The information contained in the scientific or medical journal article or reference publication should address adequate and well-controlled clinical investigations that are considered scientifically sound by experts with scientific training and experience to evaluate the safety or effectiveness of the drug or device.”).

⁷² *Id.* (“Scientific or medical information that is distributed should: be in the form of an unabridged reprint, copy of an article, or reference publication; not be marked, highlighted, summarized, or characterized by the manufacturer in any way (except to provide the accompanying disclosures discussed in this section; . . . be distributed separately from information that is promotional in nature.”).

⁷³ See Kevin Outterson, *The Last Drug Company Settlement for Off-Label Promotion*, THE INCIDENTAL ECONOMIST (Nov. 3, 2011), <http://theincidentaleconomist.com/wordpress/the-last-drug-company-settlement-for-off-label-promotion/>.

III. *SORRELL* AND OTHER CASE LAW THAT WILL CONTRIBUTE TO FUTURE COURT DECISIONS

Part III will focus on relevant case law that is likely to impact a future challenge to the off-label marketing prohibitions. Section A begins by discussing the Supreme Court decision in *Sorrell v. IMS Health*. This section considers and outlines relevant issues, rationales, and legal analyses. Section B of Part III then discusses other cases that could be influential for a future challenge.

A. *Discussion of Sorrell v. IMS Health*

i. Issue Presented

Sorrell addresses the protection of commercial speech as it relates to a drug company's ability to solicit physician prescriptions and a pharmacy's ability to profit from the information gathered about physicians.⁷⁴ The Court held that both the pharmaceutical company's right to market to physicians, as well as the pharmacy's right to distribute information about physicians, are protected by the First Amendment.⁷⁵ Pharmaceutical companies use a practice called "detailing" to market their products to physicians.⁷⁶ In order to make their marketing efforts more efficient, drug companies often purchase information about a physician's prescription practices.⁷⁷

In 2007, Vermont enacted legislation to curb this practice, believing that sales of this type of private information were dangerous to the public.⁷⁸ The Vermont law proscribed selling, disclosing, and using pharmacy records if they contain physician prescription practices.⁷⁹ Except for a limited number of exceptions, the sale or disclosure of this information by pharmacies for marketing, nor is the information lawfully used by pharmaceutical manufacturers or marketers for marketing efforts.⁸⁰ Limited circumstances include when a prescriber consents to use of the information.

Lower courts were at odds about the legality of this legislation. The U.S. District Court for the District of Vermont denied to provide relief; the court determined the legislation was a permissible use of the State's police power for the protection of the health, safety, and

⁷⁴ *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2659 (2011).

⁷⁵ *Id.*

⁷⁶ *Id.*

⁷⁷ *Id.* at 2659–60.

⁷⁸ *Id.* at 2660.

⁷⁹ *Id.* at 2660 (citing VT. STAT. ANN., tit. 18, § 4631 (Supp. 2010)).

⁸⁰ *Id.*

welfare of its citizens.⁸¹ The U.S. Court of Appeals for the Second Circuit reversed and remanded, finding that the law presented an unjustified burden on First Amendment speech interests.⁸² The Supreme Court affirmed, holding that the Vermont law imposed speaker- and content-based restrictions on speech.⁸³

ii. Determining a Level of Scrutiny

One of the more interesting aspects of *Sorrell* was the Court's decision not to use the *Central Hudson* test for commercial speech.⁸⁴ Instead, the Court decided that the regulation should be considered both a content- and speaker-based regulation on its face.⁸⁵ The law, by singling out participants in the pharmaceutical industry as prohibited recipients of the prescriber identified information, created a speaker-based restriction.⁸⁶ Additionally, because the legislation proscribed the information's use for "marketing," but no other purposes, the law also constituted a content-based restriction.⁸⁷ Each of these findings—speaker- and content-based prohibitions—trigger heightened judicial review requiring the state to show that the legislation directly advances a substantial interest, and that the legislation is narrowly drawn to achieve those ends.⁸⁸ Under the level of scrutiny required for content-based restrictions, the state must also show that there is a proportional relationship between the state's asserted purpose and the subsequent burden on speech.⁸⁹

iii. Court's Findings

The *Sorrell* Court held that the State was unable to withstand scrutiny with its asserted government interests: first, medical privacy (encompassing physician confidentiality, protection of physician harassment, and maintenance of physician patient relationship) and, second, improved public health and reduced healthcare costs.⁹⁰ The

⁸¹ *Sorrell v. IMS Health, Inc.*, 631 F. Supp. 2d 434, 435 (D.Vt. 2009).

⁸² *Sorrell v. IMS Health, Inc.*, 630 F.3d 263, 282 (1st Cir. 2010).

⁸³ *Sorrell*, 131 S. Ct. at 2672.

⁸⁴ *Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557 (1980). The *Central Hudson* test requires 1) speech be legal and not misleading 2) the government has a substantial interest, 3) the interest is directly advanced, and 4) the burden on speech is proportionally related to the State interest. *Id.* at 564.

⁸⁵ *Sorrell*, 131 S. Ct. at 2663.

⁸⁶ *Id.*

⁸⁷ *Id.*

⁸⁸ *Id.*

⁸⁹ *Id.* at 2664.

⁹⁰ *Id.* at 2668.

Court rejected the first purpose—a need for medical privacy.⁹¹ The Court also believed that this end could have been reached in a number of less restrictive ways.⁹² Additionally, the Court rejected the proposed purpose cited by the State. The State contended that the legislation was meant to prevent harassment of physicians.⁹³ The Court rejected this interest, noting that physicians intending to limit pharmaceutical detailing and marketing efforts at their practice could have merely placed signs warning marketers that solicitation was not wanted.⁹⁴ Finally, the Court rejected the State’s assertion that the law was designed to maintain appropriate physician-patient relationships.⁹⁵ In a forceful statement, the Court referred to *Brandenburg v. Ohio*, stating that “if pharmaceutical marketing affects treatment decisions, it does so because doctors find it persuasive [T]he fear that speech might persuade provides no lawful basis for quieting it.”⁹⁶

Next, the Court dismissed the State’s contention that the law advances public policy goals by lowering healthcare costs because the law did not advance these substantial interests in a permissible way.⁹⁷ When legislation infringes on speech as drastically as the Vermont law did, it must be drafted in a narrow manner that directly achieves the state’s ends.⁹⁸

As a result of these observations, the majority held that the law was unduly broad, with burdens on speech that outweighed the benefits of the intended government interests.⁹⁹ This result demonstrates that states attempting to restrict the marketing practices of pharmaceutical companies, and of other producers of healthcare information, will have to craft their legislation in a speech neutral manner. Further, the Court noted that the result of this case would not have been different had the law been analyzed using the *Central Hudson* framework,¹⁰⁰ as will likely be seen in future off-label

⁹¹ *Sorrell*, 131 S. Ct. at 2668–70.

⁹² *Id.*

⁹³ *Id.* at 2669–70.

⁹⁴ *Id.* at 2670.

⁹⁵ *Id.* at 2670.

⁹⁶ *Id.* (citing *Brandenburg v. Ohio*, 395 U.S. 444, 447 (1969)).

⁹⁷ *Sorrell*, 131 S. Ct. at 2670.

⁹⁸ *Id.*

⁹⁹ *Id.*

¹⁰⁰ *Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm. of N.Y.*, 447 U.S. 557, 564 (1980) (holding that restrictions on commercial speech do not violate the First Amendment if: (1) the speech is lawful and non-misleading, (2) the government has a substantial interest in regulating the speech, (3) the regulation directly advances

marketing challenges.¹⁰¹ Most importantly for the issue of off-label marketing, the majority seemed extremely sympathetic to the position that, in the context of commercial marketing, truthful information should not be blocked by a state.¹⁰²

B. Other Relevant Case Law to an Eventual First Amendment Challenge of the Off-Label Marketing Regulatory Scheme.

Challenging off-label marketing practices is not an entirely new concept. These challenges, however, have not yet reached the Supreme Court.¹⁰³ In the future, the *Sorrell* opinion will serve as a powerful resource for manufacturers challenging prosecution under the FDCA and FCA. In fact, the Second Circuit Court of Appeals relied heavily on *Sorrell* when the court decided *United States v. Caronia*.¹⁰⁴ Before moving on to discuss the basis of a future challenge, it is important to note some previous challenges of off-label marketing regulations.

i. *Washington Legal Foundation v. Friedman*

In the 1998 case *Washington Legal Foundation v. Friedman*,¹⁰⁵ the U.S. District Court for the District of Columbia found that the federal off-label marketing guidance documents were a violation of corporate First Amendment rights to free speech.¹⁰⁶ The court analyzed the First Amendment issue using the *Central Hudson* framework for commercial speech.¹⁰⁷ The court first determined that the speech at issue was commercial.¹⁰⁸ The court then scrutinized whether the FDA guidelines directly advanced a “substantial” government interest.¹⁰⁹

the government interest, and (4) there are not less restrictive alternatives).

¹⁰¹ See *Sorrell*, 131 S. Ct. at 2664.

¹⁰² See *id.*

¹⁰³ See, e.g., *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998); *Greater Access to Generic Drugs: New FDA Initiatives to Improve the Drug Review Process and Reduce Legal Loopholes*, *supra* note 7.

¹⁰⁴ *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012).

¹⁰⁵ *Wash. Legal Found.*, 13 F. Supp. 2d at 51.

¹⁰⁶ *Id.* at 74.

¹⁰⁷ *Id.* at 65. The court’s use of the *Central Hudson* standard is contrary to what is expected in future challenges to the FDA guidelines regarding off-label marketing. *Id.* at 65. Instead, similar to the position taken in *Sorrell*, courts will likely interpret the FDA guidelines as “content-based” and “speaker-based” restrictions on speech. *Sorrell*, 131 S. Ct. at 2663. The court will likely move directly to a strict scrutiny analysis that requires a finding of a “compelling” government interest that is “directly” related to achieving that purpose. *Id.* at 2668–69.

¹⁰⁸ *Wash. Legal Found.*, 13 F. Supp. 2d at 51.

¹⁰⁹ *Id.* at 65.

The FDA attempted to justify the regulations, claiming that the restrictions were a valid use of the State's police power to protect public health and safety.¹¹⁰ The State asserted two substantial interests that it believed the FDA guidance documents directly advanced¹¹¹: first, ensuring that physicians received accurate and unbiased information that permits them to make educated treatment decisions,¹¹² and second, ensuring that companies seek approval for previously unapproved uses of their drugs when approved drugs have unapproved uses.¹¹³ The court found that the former purpose did not constitute a substantial interest, while the latter was sufficiently substantial to warrant restrictions on speech.¹¹⁴

Having found a substantial interest, the next question became whether the FDA guidance documents directly advanced the State's purpose in a material way.¹¹⁵ The court held that the guidance documents directly advanced the purpose mainly because they provided an incentive to encourage manufacturers to seek approvals for additional indications.¹¹⁶ Due to the patent laws relating to generic drugs, and the high cost of seeking FDA approval, the court found that there were few other options apart from restricting the manufacturers' marketing practices.¹¹⁷ The scope of the restriction, however, led the court to determine that the FDA guidelines were unconstitutionally extensive.¹¹⁸ The guidance documents were overly burdensome on the manufacturers' speech because significantly less

¹¹⁰ See *id.* at 57.

¹¹¹ *Wash. Legal Found.*, 13 F. Supp. 2d at 69.

¹¹² *Id.* at 69. Ultimately, the court held that the purpose of protecting doctors from making misinformed decisions was not a substantial interest. *Id.* This holding was based on the fact that physicians are highly sophisticated and capable of making well thought out, knowledgeable treatment decisions. *Id.* The paternalistic approach of protecting doctors was not valid; the court felt that doctors would be better equipped by receiving as much information as possible to make an informed treatment decision. *Id.*

¹¹³ *Id.* at 70–72. The court held that this second interest was substantially compelling, and could justify a restriction on free speech so long as it directly achieved that end. *Id.* The fact that Congress reiterated that the approval requirement must be met for all drugs, and is not subject to any exceptions, convinced the court that the government interest was substantial. *Id.* at 71.

¹¹⁴ *Id.* at 69–72.

¹¹⁵ *Id.* at 72 (“What the court must determine is whether the Guidance Documents directly advance the ‘subsequent approval’ interest: do they encourage and/or compel a drug manufacturer to submit previously approved drugs to the FDA for approval of the off-label treatments?”).

¹¹⁶ *Id.*

¹¹⁷ *Washington Legal Found.*, 13 F. Supp. 2d at 72.

¹¹⁸ *Id.* at 72–74.

intrusive means existed to accomplish the same ends.¹¹⁹ Incentive to seek approval for off-label indications remained because, even if the limitations on “independently sponsored” continuing medical education (CME) and reprint distribution were lifted, direct marketing to physicians, internally produced off-label marketing publications, and company-sponsored CME seminars would still remain unlawful.¹²⁰ The court therefore concluded that the FDA guidelines violated the First Amendment. This result, however, was short-lived, and the case was dismissed prior to reaching the Court of Appeals. While the decision set down by the district court is not binding on any other federal courts, it does offer a possible interpretation of off-label marketing regulations.

ii. *Thompson v. Western States Medical Center*

A second case, decided by the Supreme Court of the United States, addressed the issue of drug manufacturers’ commercial speech rights.¹²¹ In *Thompson v. Western States Medical Center*, the Court held that portions of the regulations set out in the Food and Drug Administration Modernization Act (FDAMA) restricting drug manufacturers from advertising, promoting, or soliciting prescriptions for certain compounded drugs constituted a violation of the First Amendment under a *Central Hudson* commercial speech analysis.¹²² The relevant provision in the FDAMA stated that drug manufacturers of compounded drugs are exempt from the rigorous FDA approval process so long as they refrain from marketing their products.¹²³ The Court delved into a *Central Hudson* analysis to

¹¹⁹ *Id.* The less intrusive means focused most heavily on mandatory disclosure. Disclosure would assuage the governments concerns with potentially misleading physicians. *Id.* Additionally, companies would still have significant incentive to seek re-approval because the decision in this case was narrow. *Id.* Direct marketing to physicians, pharmaceutical company initiated seminars, and internally produced and distributed marketing materials all fell outside the scope of this decision. *Id.*

¹²⁰ *Id.* at 73 (“[I]t is a very narrow form of manufacturer communication upon which this court is ruling in enjoining enforcement of the Guidance Documents. There still are enormous differences between the permitted marketing of on-label as opposed to off-label uses. Manufacturers still are proscribed from producing and distributing any internally-produced marketing materials to physicians concerning off-label uses, or from involvement with seminars not conducted by an ‘independent program provider.’ Nor may the drug companies initiate person-to-person contact with a physician about an off-label use. Nor may they advertise off-label uses for previously approved drugs directly to the consumer.”).

¹²¹ *Thompson v. W. States Med. Ctr.*, 535 U.S. 357 (2002).

¹²² *Id.* at 373–74.

¹²³ 21 U.S.C. § 353a(c) (2006) (“A drug may be compounded under subsection (a) of this section only if the pharmacy, licensed pharmacist, or licensed physician

determine the constitutionality of such provisions.¹²⁴ After the Court determined that the speech was lawful, the State proffered three explanations of the substantial nature of the regulations.¹²⁵ The State asserted that the regulation: (1) ensured the integrity and effectiveness of the new drug approval process and its impact on public health; (2) preserved the availability of compounded drugs for patients that have not had success with other available drugs; and (3) managed a balance between these first two objectives.¹²⁶ The Court accepted these reasons as substantial; however, it struck down the legislation because the law failed to meet the fourth prong of the *Central Hudson* analysis—that there must not be less restrictive means to achieve the stated governmental interest.¹²⁷ The Court believed that a number of speech-neutral means existed to promote the asserted government ends, and determined the provision to be unconstitutional.¹²⁸

Beyond the strict rule of law applied in *Thompson*, the Court also provided some powerful dicta that could be applicable for future challenges to the off-label marketing regulations. The Court cited a number of commercial speech cases leading up to *Thompson*, illustrating the sentiment towards commercial speech. For example, in *Virginia Board of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, the Court stated, “[i]t is a matter of public interest that [economic] decisions, in the aggregate, be intelligent and well informed. To this end, the free flow of commercial information is indispensable.”¹²⁹ Such a statement is pertinent within scientific and medical commercial speech more so than anywhere else. In an age when

does not advertise or promote the compounding of any particular drug, class of drug, or type of drug. The pharmacy, licensed pharmacist, or licensed physician may advertise and promote the compounding service provided by the licensed pharmacist or licensed physician.”). This provision was declared unconstitutional in *Thompson* and, rather than severing the section from the statute, the Court declared the entire statute unconstitutional. *Thompson*, 535 U.S. at 357.

¹²⁴ *Thompson*, 535 U.S. at 368.

¹²⁵ *Id.*

¹²⁶ *Id.*

¹²⁷ *Id.* at 371 (“[I]f the Government could achieve its interests in a manner that does not restrict, or that restricts less speech, the Government must do so.”).

¹²⁸ *Id.* at 372–73. The Court noted the government could have used at least three other mechanisms to achieve patient safety while still making the compounding practice available to needy patients. *Id.* They noted a ban on commercial scale manufacturing, restrictions on preemptive production of compounding products in expectation of future prescriptions, and prohibitions on wholesale sales of compounding products to other licensed individuals. *Id.*

¹²⁹ *Id.* at 366 (quoting *Va. Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 765 (1976)) (internal quotation marks omitted).

patients increasingly seek information about their treatment and illnesses, it is important this medical information be available to them. Again, in assessing the role of government in determining whether commercial speech has a positive or negative effect on the public, the Court noted that “the general rule is that the speaker and the audience, not the government, assess the value of the information presented.”¹³⁰ The dissent pointed out that there is a government interest in the prevention of marketing efforts that persuade doctors to treat their patients using a certain marketed protocol.¹³¹ The majority vehemently rejected the point, however, stating that “[t]he First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good.”¹³² Thus, the paternalistic legislative approach is a method that the Court seems to strongly disfavor.

iii. *United States v. Caronia*

In 2012, the U.S. Court of Appeals for the Second Circuit issued an already controversial decision in *United States v. Caronia*, a decision that cut one of the enforcement legs out from underneath the FDA.¹³³ The court determined that the prosecution of truthful speech through the FDCA’s misbranding provisions is unconstitutional and a violation of the First Amendment.¹³⁴

Defendant Caronia worked as a detailer for Orphan Medical, Inc., the manufacturer of the drug Xyrem.¹³⁵ Xyrem was approved by the FDA for only two medical indications: cataplexy and excessive day-time sleepiness associated with narcolepsy.¹³⁶ During a meeting with a physician, Caronia stated that the drug could be used to treat restless leg syndrome and pain associated with fibromyalgia.¹³⁷ The Government recorded this conversation, and eventually prosecuted

¹³⁰ *Thompson*, 535 U.S. at 367 (quoting *Edenfield v. Fane*, 507 U.S. 761, 767 (1993)).

¹³¹ *Id.* at 382–85 (Breyer, J., dissenting). The ideal process for prescription practices is that the original motivation for the need for the prescription comes from the physician, flowing from physician to patient to pharmacist. *Id.* at 382. The concern is that advertising will produce a system that originates a process of pharmacist to patient to doctor. *Id.* Many studies have shown that physicians will acquiesce to patients’ requests for specific medications. *Id.* at 383–84.

¹³² *Id.* at 375 (quoting *44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 503 (1996)) (internal quotation marks omitted).

¹³³ *United States v. Caronia*, 703 F.3d 149, 152 (2d Cir. 2012).

¹³⁴ *Id.*

¹³⁵ *Id.* at 155–56.

¹³⁶ *Id.*

¹³⁷ *Id.* at 156.

Caronia for violating the FDCA's misbranding provisions.¹³⁸

In its decision, the court focused on the State's contention that the promotional speech itself constituted impermissible misbranding.¹³⁹ The court rejected the State's argument that the promotional speech was not criminalized in itself; instead the court found that the speech only served as evidence of intent to misbrand.¹⁴⁰ The court found that the misbranding provisions of FDCA represented both content- and speaker-based restrictions.¹⁴¹ The provisions established a content-based restriction because they favored truthful on-label speech over truthful off-label speech.¹⁴² The provisions established a speaker-based restriction because physicians can promote off-label uses with impunity but detailers are restricted from making the same truthful promotions.¹⁴³

Although suggesting that strict scrutiny should apply to the provisions, the court employed the lesser *Central Hudson* test.¹⁴⁴ The court determined that the State's interests were not directly advanced, nor were they narrowly drawn, to achieve the State's objectives.¹⁴⁵ The court rejected State's interest in protecting the integrity of the FDA approval process by ensuring manufacturers have an incentive to seek re-approval.¹⁴⁶ The court reasoned that the simple fact that off-label prescribing is lawful undermines the State's asserted interest that off-label restrictions are needed to encourage companies to seek re-approval.¹⁴⁷ The majority also held that the regulations were not narrowly drawn because other options, such as warnings for drugs prescribed off-label, ceilings for the amounts of a drug that can be prescribed off-label, or outright prohibition of off-label prescribing, would all appropriately achieve the State's interest.¹⁴⁸

Caronia gives rise to a number of interesting evaluations. First, the court relied heavily on the Supreme Court's decision in *Sorrell* to assist in the determination that the provisions represented a content-

¹³⁸ *Id.* at 156–57.

¹³⁹ *Caronia*, 703 F.3d at 160.

¹⁴⁰ *Id.* at 161–62.

¹⁴¹ *Id.* at 165.

¹⁴² *Id.* at 165–69.

¹⁴³ *Id.* at 165.

¹⁴⁴ *Id.* at 165.

¹⁴⁵ *Caronia*, 703 F.3d at 166–69.

¹⁴⁶ *Id.* at 166–68.

¹⁴⁷ *Id.*

¹⁴⁸ *Id.* at 168.

and speaker-based restriction.¹⁴⁹ As noted above, in *Sorrell*, the Court's finding that the Vermont statute was a content- and speaker-based restriction represented a novel approach to a First Amendment challenge brought on behalf of a commercial company.¹⁵⁰ Second, the court's decision to disregard a strict scrutiny standard, although applicable, and instead strike down the provision under the less-onerous *Central Hudson* test, was fairly unexpected.¹⁵¹ Finally, the scope of the *Caronia* decision is admittedly narrow by only making a determination on the constitutionality of prosecution under the FDCA's misbranding provisions, the court did not in any way address the constitutionality of enforcement of off-label marketing violations under the FCA.¹⁵² These observations will surely play a substantial role in any potential future appeal to the Supreme Court, but at this point it is not known if the case will rise to the nation's highest court.

The cases above establish a valid argument for both sides in this debate. The rejection of the State's interest, to encourage companies to seek reapproval for off label indications, in *Caronia* is contrary to the District of D.C.'s support of the same interest in *Washington Legal Foundation*. Whether the Supreme Court will follow suit is unclear; the following section provides an overview of what the Supreme Court's analysis might look like based upon these and other considerations.

V. THE LIKELY ARGUMENTS AND SUPREME COURT CONSIDERATIONS FOR THE POTENTIAL CHALLENGE AGAINST THE CURRENT REGULATORY MECHANISM WITH PARTICULAR ATTENTION TO *SORRELL*'S IMPACT ON THE COURT'S ANALYSIS

Sorrell is relevant to future challenges to off-label marketing restrictions for a number of reasons. First, the case provides important dicta that provide an intimate look at the Court's thoughts on commercial speech within the context of the healthcare industry. Second, *Sorrell* provides an analysis of a free speech challenge that ultimately received heightened scrutiny. *Sorrell* will provide an analogous opinion if a future challenge requires application of heightened scrutiny. The *Sorrell* opinion also provides a comparison to the *Central Hudson* framework that the courts could easily apply to the off-label promotion restrictions. Finally, the Court in *Sorrell*

¹⁴⁹ See generally *id.* at 163–64.

¹⁵⁰ See *infra*, Part III.A.

¹⁵¹ *Caronia*, 703 F.3d at 164.

¹⁵² *Cf. id.* at 164.

clarified that it is unlikely that the ruling will be any different whether the case proceeds on a scientific speech or commercial speech scrutiny framework.¹⁵³

The misbranding provisions of the FDCA and the provisions under the FCA do not pose facially burdensome speech restrictions, but enforcement of off-label restrictions under these provisions as applied creates both content and speaker-based restrictions.¹⁵⁴ For example, the only possible violator of the FDCA's regulation on the "intended use" is an agent of a company speaking on behalf of the company's product.¹⁵⁵ The same information that would trigger a violation if mentioned by a corporate agent would be perfectly lawful if discussed or disseminated by any unconnected physician, researcher, scholar, or businessman.¹⁵⁶ This is an analogous situation to that presented in *Sorrell*. There, the Court noted that "Vermont's law thus has the effect of preventing detailers—and only detailers—from communicating with physicians in an effective and informative manner."¹⁵⁷ Similarly, prosecution guidelines under FDCA restrict only pharmaceutical manufacturers and their agents from communicating truthful off-label information about their products to physicians.¹⁵⁸

Additionally, the FDA regulation of off-label promotion could potentially be deemed to create a content-based restriction on speech. As stated in *Sorrell*, "[c]ontent-neutral speech regulations are those that are justified without reference to content of regulated speech."¹⁵⁹ In the case of off-label restrictions, the law is enforced to favor speech relating to on-label drug use and disfavors speech pertaining to off-label medications.¹⁶⁰ Similar to the findings of *Sorrell* and *Caronia*, by burdening specific content of speech—namely off-

¹⁵³ *Sorrell v. IMS Health, Inc.*, 131 S. Ct. 2653, 2667 (2011).

¹⁵⁴ *See Caronia*, 703 F.3d at 164.

¹⁵⁵ *Id.* at 165.

¹⁵⁶ *See* U.S.C. § 352(a) (2006). The regulations permit physicians, researchers, publications, and the general public to endorse the use of pharmaceuticals for off-label indications. *Id.* This permission is not expressly given; however, it is inferred because off-label marketing is patrolled using labeling restrictions. *Id.* Because pharmaceutical companies are the only manufacturers of these labels, they are the only entities that are restricted from promoting the off-label uses. *Id.*; *see also Use of Approved Drugs for Unlabeled Indications*, 12 FDA DRUG BULL. 4 (1982), available at http://www.circare.org/fda/fdadrugbulletin_041982.pdf.

¹⁵⁷ *Sorrell*, 131 S. Ct. at 2663.

¹⁵⁸ *See* *United States v. Caronia*, 703 F.3d 149, 166–67 (2d Cir. 2012).

¹⁵⁹ *Sorrell*, 131 S. Ct. at 2664. (quoting *Renton v. Playtime Theatres, Inc.*, 475 U.S. 41, 48 (1986)) (internal quotation marks omitted).

¹⁶⁰ 21 C.F.R. §§ 201.100(d)(1) (2006).

label uses of pharmaceutical products—the Court will likely conclude that the provisions of both the FDCA and FCA are content-based restrictions.

If the Supreme Court determines that the FCA or FDCA creates either a content- or speaker-based restriction, the government would be forced to meet heightened scrutiny standards; this would require the government to show the regulation serves a compelling state interest, the regulation is directly crafted to serve that interest, and the regulation does not burden speech more than needed to achieve the state interest.¹⁶¹ Such a challenge presents significant potential for success, as less intrusive alternatives for achieving the government's asserted purposes exist.¹⁶²

If the FDA's off-label regulatory mechanisms are deemed content- or speaker-based restrictions by the Supreme Court, the probable interest that the state will assert is its desire to prevent companies from seeking limited approval of a drug for a specified use, and then marketing that drug for a host of unproven uses.¹⁶³ For example, Drug Manufacturer X creates "Drug Z" and seeks approval for treatment of high blood pressure. Drug Manufacturer X also believes that the drug can be used to treat anxiety, erectile dysfunction, mood stabilization, and a host of other ailments. The company would be free to market "Drug Z" to physicians for any of these reasons without ever completing the large-scale clinical trial studies required to obtain initial FDA approval. This process poses a potentially dangerous threat to public safety that many regulators believe should be restricted.¹⁶⁴

The final step the Court will need to consider is whether less speech restrictive alternatives can achieve this state interest. It has been determined by at least one court, that a number of less intrusive means exist to achieve the government's asserted end. For example, in *Caronia* the court determined that warnings on off-label drugs, ceilings for the amounts of a drug that can be prescribed off-label, or outright prohibition of off-label prescribing, would all appropriately achieve the state's interest.¹⁶⁵ These alternatives all represent feasible options, and the most useful mechanism, a quota system, is evaluated in more detail below.¹⁶⁶

¹⁶¹ *Sorrell*, 131 S. Ct. at 2664.

¹⁶² See *infra* Part IV.A.

¹⁶³ See *Wash. Legal Found. v. Friedman*, 13 F. Supp 2d 51, 72 (D.D.C 1998).

¹⁶⁴ *Stafford*, *supra* note 2; see also *Dresser*, *supra* note 4.

¹⁶⁵ *United States v. Caronia*, 703 F.3d 149, 168 (2d Cir. 2012).

¹⁶⁶ *Infra* Part VI.

Although there is significant evidence to indicate that the Court will find this speech to be scientific, it is possible that the Court will analyze the off-label promotion restrictions under the *Central Hudson*—commercial speech—guidelines.¹⁶⁷ As evidenced by the *Caronia* decision, the result is largely the same whether the court utilizes the *Central Hudson* framework or the heightened scrutiny standard used in *Sorrell*.¹⁶⁸ Under the heightened scrutiny analysis, any plaintiff is likely to point out the multitude of less invasive methods to achieve the asserted government interest. The Court's analysis is likely to hinge on whether alternatives exist to encourage companies to seek full FDA approval of off-label indications.¹⁶⁹ The list of alternative options proposed in *Caronia* provides future plaintiffs with a good start, as the Court could potentially consider a quota system as a potential replacement for the current regulatory structure.¹⁷⁰

These considerations, taken in combination with *Sorrell*'s incredibly sympathetic dicta regarding the protection of free speech in the context of educating physicians, seem to indicate that the Supreme Court will prefer less speech-restrictive alternatives in the future.¹⁷¹ In *Sorrell*, the Court rejected the argument that granting detailers greater latitude would negatively affect the treatment of patients.¹⁷² In fact, this gives rise to the most telling sentiment of the Court; the majority stated, “[i]f pharmaceutical marketing affects treatment decisions, it does so because doctors find it persuasive.”¹⁷³ The Court seems inclined to allow physicians to distill what information is relevant to medical treatment. The Court followed by again noting, “[t]here are divergent views regarding detailing and the prescription of brand-name drugs. Under the Constitution, resolution of that debate must result from free and uninhibited

¹⁶⁷ *Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm. of N.Y.*, 447 U.S. 557, 564 (1980).

¹⁶⁸ *Caronia*, 703 F.3d 149; *Sorrell v. IMS Health, Inc.*, 131 S. Ct. 2653, 2664 (2011).

¹⁶⁹ The plaintiff's argument is likely to mention some of the arguments presented in *Thompson v. W. States Med. Ctr.*, 535 U.S. 357 (2002), a precedential case that noted less intrusive means could include: prohibition on the sales of certain products to other licensed individuals, restrictions on preemptive production of compounding products, and bans on manufacturing.

¹⁷⁰ *Caronia*, 703 F.3d at 168.

¹⁷¹ *Sorrell*, 131 S. Ct. at 2670–71 (citing *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 374 (2002). (“[T]he fear that people would make bad decisions if given truthful information cannot justify content based burdens on speech.”)).

¹⁷² *Id.* at 2669–71.

¹⁷³ *Id.*

speech.”¹⁷⁴ The sentiments of the Court are tempered by the ability of the government to achieve its interest in a less intrusive manner. The threshold issue moving forward will be whether there are any speech-neutral alternatives to achieve the government interest.

VI. PRESCRIPTION DRUG QUOTA SYSTEMS AS A SPEECH NEUTRAL
ALTERNATIVE FOR ACHIEVING THE STATE’S SUBSTANTIAL INTEREST:
UTILIZING THE PRESCRIPTION DRUG MONITORING PROGRAMS AS A
ROADMAP FOR IMPLEMENTATION

The government’s primary underlying interest for maintaining off-label marketing restrictions for pharmaceutical manufacturers—to encourage companies to seek full FDA approval for off-label indications—can be achieved without burdening corporate speech rights. Establishing a quota system is a realistic alternative to the current regulatory structure. For the purpose of this Comment, the proposed quota system would serve as a ceiling for drug manufacturers; when a manufacturer sells a certain number, or percentage, of prescriptions for an off-label indication, the company would be required to seek FDA approval for this off-label indication.

Given the current state of networking technology and prescription monitoring program laws, establishing a realistic infrastructure that would enable the FDA to track the number of prescriptions issued for off-label indications is a feasible speech-neutral option designed to quell the above concern.¹⁷⁵ Prescription Drug Monitoring Programs (PDMPs) have made substantial advancements within the last decade.¹⁷⁶ Currently, 49 states have PDMP laws, 41 of which have operational programs; this is a three-fold increase from the 16 states that had passed PDMP legislation in 2001.¹⁷⁷ Technology developed by the American Society for Automation in Pharmacy (ASAP) represents the uniform standard for PDMPs.¹⁷⁸ Recent versions of ASAP system have increased the number of data fields it collects, making inclusion of the off-label nature of the prescription possible using this technology.¹⁷⁹ While the rapid expansion of PDMPs is encouraging, the government would

¹⁷⁴ *Id.* at 2671.

¹⁷⁵ THOMAS CLARK ET AL., PRESCRIPTION DRUG MONITORING PROGRAMS: AN ASSESSMENT OF THE EVIDENCE FOR BEST PRACTICES 5 (Sept. 20, 2012), available at http://www.pdmpexcellence.org/sites/all/pdfs/Brandeis_PDMP_Report.pdf.

¹⁷⁶ *Id.*

¹⁷⁷ *Id.*

¹⁷⁸ *Id.* at 4.

¹⁷⁹ *Id.* at 13.

need to implement these PDMPs on a national scale. It appears that this is possible.

Currently, the shortcomings of the reporting infrastructure are too great to easily incorporate the inclusion of an off-label indication dataset; however, adoption of the most recent ASAP software would permit inclusion of off-label tracking.¹⁸⁰ Despite this ability, some shortcomings of the current PDMP infrastructure should be noted for the purpose of understanding how the system should be altered. First, the use of electronic prescribing is not yet the industry standard. New York did, however, pass legislation in 2012 that mandated all controlled substance prescriptions be issued electronically by the end of 2014.¹⁸¹ This is the first mandatory E-prescription law in the country.¹⁸² The program requires reporting of more than ten different data fields to the system.¹⁸³ Second, not all states adopt identical PDMP legislation, making the fluidity of amending the laws cumbersome at a national level.¹⁸⁴ The Alliance of States with Prescription Monitoring Programs established a Model PMP Act in 2010 that can potentially serve as the national standard.¹⁸⁵ Third, two-thirds of reporting programs do not require reporting for drugs that are not Schedule II controlled substances.¹⁸⁶ The reporting system would have to be mandatory for all prescription drugs to appropriately address the off-label prescription issue.

A federal law establishing a national database capable of handling the reporting of off-label prescriptions would need to be passed for a quota system to become feasible. The law should have a couple key characteristics. First, a national database or, at a minimum, a system that creates uniformity among all state data collection procedures, must be implemented.¹⁸⁷ This system would have to require tracking of all prescriptions. Second, the federal

¹⁸⁰ *Id.*

¹⁸¹ Med. Soc'y of the State of N.Y., I-STOP Law: MSSNY Working to Assure MSSNY Physician Participation on DOH Work Group on Prescription Pain Medication Awareness, *online available at*: http://www.mssny.org/mssnycfm/mssnyeditor/File/2013/Home/I-STOP_010813/I_STOP_MEMO.pdf.

¹⁸² *Id.*

¹⁸³ N.Y. Senate, Legislative Drafting Commission, 12123-11-2, Program Bill #39, Part (A) § 3343-a(b).

¹⁸⁴ CLARK ET AL., *supra* note 175, at 13.

¹⁸⁵ *Prescription Monitoring Program Model Act 2010 Revision*, ALLIANCE OF STATES WITH PRESCRIPTION MONITORING PROGRAMS (June 28, 2010), *available at* pmpalliance.org/pdf/PMPModelActFinal20100628.pdf.

¹⁸⁶ CLARK ET AL., *supra* note 175, at 14.

¹⁸⁷ *Id.* at 13.

government would likely need to implement, and require use of, nationally standardized prescription pads, or e-script systems. These prescription forms should include a mechanism to record that the drug is being prescribed for an off-label indication.¹⁸⁸ These are not unrealistic requirements, particularly if adoption of modern ASAP technology is made the national standard.¹⁸⁹ One potential method for ensuring uniform adoption of these procedures is incentivizing state participation through the Federal Harold Rogers Prescription Drug Monitoring Program.¹⁹⁰ By refusing to provide monetary support to states adopting noncompliant versions of the PDMP's uniform structure, it might provide enough incentive for those states to adopt the uniform infrastructure.

A reporting system, as outlined above, would permit the FDA to track the number of prescriptions of a certain drug that could trigger obligatory re-approval of the drug for that indication. This mandatory re-approval would likely achieve the state-interest in retaining the integrity of the FDA approval process. For example, Drug X has been given initial approval for treatment of high blood pressure. Doctors subsequently discover that it is useful for treating anxiety. The pharmaceutical company then begins soliciting the prescription of the drug for the treatment of anxiety—an action that is currently prohibited, but would not be restricted if the Supreme Court abolishes off-label marketing restrictions. The physician then prescribed the drug off-label to treat anxiety. After approximately one year, it is clear that twenty-five percent of all prescriptions for Drug X are for the treatment of anxiety. The company would then be required to initiate the FDA re-approval process for the treatment of anxiety—to alter the product's approved labeling. If the company failed to do so, it would be subject to heavy penalties.

A quota system represents a realistic alternative to the current system. Although moderate barriers exist to the establishment of a quota system, these hurdles are not prohibitive. Accordingly, when consideration of this issue reaches the Supreme Court, the existence of speech neutral alternatives is likely to be the Government's greatest liability.

¹⁸⁸ *Id.* at 13.

¹⁸⁹ *Id.* at 4.

¹⁹⁰ *Harold Rogers Prescription Drug Monitoring Program*, BUREAU OF JUSTICE ASSISTANCE (Mar. 20, 2012), <http://www.ojp.usdoj.gov/BJA/grant/prescripdrugs.html>.

VII. CONCLUSION

The off-label promotion issue is quickly coming to a head, and is likely to find its way up to the Supreme Court in the future. Based on the current state of the law, seen in *Washington Legal, Thompson*, and *Caronia*, as well as the relevant excerpts from *Sorrell*, it is likely that the off-label promotion regulation is in serious jeopardy. It is important to keep in mind the importance of public health, safety, and welfare when considering a revision of the laws. Developing systems to identify misleading assertions is among the most important aspects of the law. Additionally, creating incentives for companies to seek FDA approval for off-label indications is crucial.

While removing restrictions carries potential for corporate abuse, the valuable contribution that free-flowing information could contribute to patient safety might outweigh this danger. Currently, it takes nearly twenty years for pharmaceuticals to get from “bench to bedside,” leaving desperate patients without potential treatment options because of bureaucratic red tape. Removal of off-label marketing restrictions will increase the availability of data regarding potential uses of certain drugs. Lifting the ban will also give the pharmaceutical companies incentive to perform research to support the use of their products for new indications.

Sorrell may not have been the ground-breaking First Amendment case for which many pharmaceutical companies were hoping, but it certainly shed insight into the sentiments of the Court. The case hinted at the possibility that the Court might not even need to approach the off-label marketing issue from a commercial speech (*Central Hudson*) vantage point; rather the Court might move directly into heightened scrutiny based on the guideline’s establishment of content and speaker based restrictions. In any event, the coming Supreme Court sessions will likely see a challenge to the off-label marketing regulations because of their undue infringement on corporate speech rights.

The outcome of these cases will depend heavily on an analysis of feasible alternatives to the speech restrictive FDA guidelines. While speech neutral quota systems would ultimately achieve the government’s compelling purpose, the system’s success rests heavily on important changes that must be made to the federal healthcare infrastructure. If the Court deems such an alternative adequate, the FDA guidelines restricting off-label marketing could be overturned, a change that will likely send the FDA and legislators into a scramble to create workable regulations.