

# A Spoonful of Free Speech Helps the Medicine Go Down: Off-Label Speech & the First Amendment

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*ABSTRACT: For over a decade, drug manufacturers have maintained that Food and Drug Administration (“FDA”) regulations restricting their ability to promote prescription drugs for off-label uses violate the First Amendment. Courts faced with First Amendment challenges to the FDA’s off-label speech restrictions have been reluctant to declare them facially unconstitutional. These courts fear that declaring such restrictions facially unconstitutional will undermine the FDA’s process for assessing and approving new drugs to the public’s detriment. However, relying in part on the recent Supreme Court decision in Sorrell v. IMS Health Inc., the Second Circuit held in United States v. Caronia that the FDA’s speech restrictions, at least in some cases, violate drug manufacturers’ First Amendment rights.*

*Sorrell raised serious questions as to whether a court should apply strict scrutiny in addressing the constitutionality of the FDA’s off-label speech restrictions. In light of these questions, this Note argues that courts addressing First Amendment challenges should not interpret Sorrell to require strict scrutiny in the off-label context and should continue to adjudge the FDA’s off-label restrictions under Central Hudson’s less-exacting, commercial speech framework. This Note concludes that, even by Central Hudson’s standard, the FDA’s off-label restrictions violate drug manufacturers’ First Amendment rights, and it proposes several ways the FDA and Congress may bring current law into conformity with the First Amendment.*

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## I. INTRODUCTION

For over a decade, drug manufacturers have argued that Food and Drug Administration (“FDA”) regulations restricting manufacturers’ ability to promote off-label<sup>1</sup> uses of prescription drugs violate manufacturers’ First Amendment rights.<sup>2</sup> Drug manufacturers and individuals have repeatedly raised First Amendment challenges to the FDA’s regulations.<sup>3</sup> In the district courts, drug manufacturers have obtained both favorable and unfavorable rulings.<sup>4</sup> However, until recently, the FDA forestalled drug manufacturers from obtaining a favorable circuit court decision by “deftly maneuver[ing] around” appeals, either by forcing settlements<sup>5</sup> or modifying interpretations of regulations and guidance documents to make challenges “disappear[.]”<sup>6</sup>

*United States v. Caronia*, however, did not disappear.<sup>7</sup> Rather, in *Caronia*, the Second Circuit rendered a 2–1 pro-manufacturer decision.<sup>8</sup> In doing so, the Second Circuit fulfilled drug manufacturers’ and free-speech proponents’ hopes that *Caronia* would produce groundbreaking precedent

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1. The term “off-label” denotes the practice of prescribing drugs for uses not “approved by the FDA.” Randall S. Stafford, *Regulating Off-Label Drug Use—Rethinking the Role of the FDA*, 358 NEW ENG. J. MED. 1427, 1427 (2008). The FDA requires that a drug’s label include all of the drug’s FDA-approved uses. See 21 U.S.C. § 355(d) (2012). Thus, a physician who prescribes a drug for an unapproved use prescribes a drug for a use that is necessarily “off-label.” Conversely, the term “on-label” denotes the practice of prescribing a drug for an FDA-approved use.

2. See Jacqueline R. Berman, *First Amendment Off-Label Promotion Cases Work Their Way Through the Courts*, J. HEALTH CARE COMPLIANCE, Mar.–Apr. 2012, at 33; A. Elizabeth Blackwell & James M. Beck, *Drug 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); Jose Sierra, *The First Amendment Battle over Off-Label Promotion*, PHARMARISC.COM (Dec. 14, 2011), <http://pharmarisc.com/2011/12/off-label-promotion-as-a-government-weapon>; Sally Wang, *Let the Arms Race End: Opening the Door to Flexible Drug Marketing Regulation Through an IP Justification*, JOLT DIGEST (May 25, 2012), <http://jolt.law.harvard.edu/digest/digest-comment/let-the-arms-race-end-opening-the-door-to-flexible-drug-marketing-regulation-through-an-ip-justification>.

3. See, e.g., *United States v. Caronia*, 703 F.3d 149, 160 (2d Cir. 2012) (using the First Amendment as a defense in a criminal misbranding case); *United States v. Caputo*, 288 F. Supp. 2d 912, 919 (N.D. Ill. 2003) (same); *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51, 54 (D.D.C. 1998) (seeking, in a declaratory judgment action, an injunction preventing the FDA from enforcing off-label policies); Memorandum of Law in Support of Plaintiff’s Motion for Preliminary Injunction at 11, *Par Pharm., Inc., v. United States*, No. 1:11-cv-01820 (D.D.C. filed Oct. 14, 2011) [hereinafter *Par-Pharm Plaintiff’s Memorandum*] (seeking, in a declaratory judgment action, an injunction preventing the FDA from enforcing off-label regulations).

4. Compare *Caputo*, 288 F. Supp. 2d at 922 (holding that the FDA’s off-label promotion restrictions do not violate the First Amendment), with *WLF I*, 13 F. Supp. 2d at 73–74 (holding that the FDA’s guidance documents violate the First Amendment).

5. Sierra, *supra* note 2.

6. *Wash. Legal Found. v. Henney*, 202 F.3d 331, 335 (D.C. Cir. 2000); see also Sierra, *supra* note 2.

7. See generally *Caronia*, 703 F.3d 149.

8. See *id.* at 168–69; see generally Blackwell & Beck, *supra* note 2.

in the world of off-label promotion.<sup>9</sup> Over a strong dissent, the *Caronia* court held the government's use of the Food Drug and Cosmetic Act ("FDCA") to prosecute drug manufacturers for promoting the lawful, off-label use of FDA-approved drugs violated the First Amendment.<sup>10</sup> Although drug manufacturers won the battle in *Caronia*, the war is far from over.<sup>11</sup>

A primary point of contention in the ongoing dispute over off-label speech is the standard of scrutiny applicable to the FDA's regulations.<sup>12</sup> A recent Supreme Court decision, *Sorrell v. IMS Health Inc.*, further confused the issue by suggesting courts may need to apply strict scrutiny in addressing the constitutionality of the FDA's off-label speech restrictions while still, ultimately, assessing the constitutionality of the law in question under intermediate scrutiny.<sup>13</sup> Several commentators urge that *Sorrell* requires courts to apply strict scrutiny when reviewing the constitutionality of restrictions on off-label speech, despite the fact that commercial speech restrictions—like those the FDA imposes on drug manufacturers—are typically subject to intermediate scrutiny.<sup>14</sup> The Second Circuit's *Caronia* opinion adopted this view.<sup>15</sup> This Note demonstrates, however, that the *Sorrell* Court was uniquely concerned with viewpoint discrimination. Thus, courts reviewing First Amendment challenges to off-label speech restrictions should interpret *Sorrell* narrowly and continue to apply intermediate scrutiny to FDA regulations.

This Note addresses the First Amendment concerns implicated by the FDA's off-label speech restrictions and argues the FDA's off-label speech restrictions are unconstitutional even under intermediate scrutiny. Part II explains the impact of the FDCA and surveys the development of the commercial speech doctrine. Part III explores three First Amendment

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9. See John R. Fleder, *New Twists and Turns in Off-Label Marketing*, FDA L. BLOG (Sept. 21, 2011, 1:43 PM), [http://www.fdalawblog.net/fda\\_law\\_blog\\_hyman\\_phelps/2011/09/new-twists-and-turns-in-off-label-marketing.html](http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2011/09/new-twists-and-turns-in-off-label-marketing.html) ("One of the appellate briefs supporting Mr. Caronia's appeal was filed by the Medical Information Working Group (MIWG), a group composed of eleven major pharmaceutical companies.").

10. *Caronia*, 703 F.3d at 168.

11. See Jose Sierra, *Caronia Decided—First Amendment Protects Off-Label Speech!*, PHARMARISC.COM (Dec. 4, 2012), <http://pharmarisc.com/2012/12/caronia-decided-first-amendment-protects-off-label-speech>.

12. See *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2678 (2011) (Breyer, J., dissenting) (predicting the off-label scrutiny battle and warning against interpreting the majority's opinion broadly). Compare *Caronia*, 703 F.3d 149 (majority opinion), with *id.* at 169 (Livingston, J., dissenting).

13. See *Sorrell*, 131 S. Ct. at 2662, 2672.

14. Erin E. Bennett, Comment, *Central Hudson-Plus: Why Off-Label Pharmaceutical Speech Will Find Its Voice*, 49 HOUS. L. REV. 459, 474 (2012); cf. Donald W. Garner & Richard J. Whitney, *Protecting Children from Joe Camel and His Friends: A New First Amendment and Federal Preemption Analysis of Tobacco Billboard Regulation*, 46 EMORY L.J. 479 (1997) (examining the commercial speech doctrine in the context of tobacco advertising).

15. See *Caronia*, 703 F.3d at 163.

challenges to the FDA's off-label speech restrictions, including *United States v. Caronia*,<sup>16</sup> *Washington Legal Foundation v. Friedman*,<sup>17</sup> and *United States v. Caputo*.<sup>18</sup> Finally, Part IV argues that, post-*Sorrell*, courts addressing First Amendment challenges to the FDA's off-label speech restrictions should continue to apply intermediate scrutiny and concludes that, even under the more lenient intermediate scrutiny standard, the FDA's off-label speech restrictions are unconstitutional. This Note concludes by recommending several ways Congress or the FDA may effectively control the flow of off-label prescribing information without violating the First Amendment.

## II. STATUTORY FRAMEWORK AND THE COMMERCIAL SPEECH DOCTRINE

This Part explains the FDCA and surveys the development of the commercial speech doctrine. Subpart II.A discusses the FDCA's new drug approval process, the FDCA's misbranding provisions, and the risks and benefits associated with off-label use. Subpart II.B traces the development of the commercial speech doctrine, including a discussion of *Central Hudson Gas & Electric Corp. v. Public Service Commission of New York*,<sup>19</sup> *Thompson v. Western States Medical*,<sup>20</sup> and *Sorrell v. IMS Health Inc.*<sup>21</sup>

### A. STATUTORY FRAMEWORK: THE FOOD DRUG & COSMETIC ACT AND THE FDA

The FDA's mission is to "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."<sup>22</sup> In furtherance of that end, the FDCA authorizes the FDA to regulate drug distribution in predominantly two ways. First, the FDCA's new drug approval process requires that manufacturers demonstrate to the FDA, "through a rigorous series of pre-clinical and clinical trials, that [new drugs are] both safe and effective for each of [their] intended uses" before they may be distributed in commerce.<sup>23</sup> However, the FDA does not regulate the practice of medicine; thus, physicians are free to prescribe off-label.<sup>24</sup> Second, the misbranding provisions of the FDCA authorize the FDA to regulate prescription drug manufacturers' promotional efforts after their drugs have entered the

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16. *Id.*

17. *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51 (D.D.C. 1998).

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

19. *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557 (1980).

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

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

22. 21 U.S.C. § 393(b)(1) (2012).

23. *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51, 55 (D.D.C. 1998).

24. Historically, the FDA has avoided regulating the practice of medicine to avoid interfering with doctors' ability to address individual patient needs. Some argue the FDA lacks the statutory authority to regulate the practice of medicine altogether. See William L. Christopher, *Off-Label Drug Prescription: Filling the Regulatory Vacuum*, 48 FOOD & DRUG L.J. 247, 254 (1993).

market.<sup>25</sup> A manufacturer's failure to comply with either the new drug approval process requirements or the FDCA's misbranding provisions is a criminal offense.<sup>26</sup> The following Subparts illustrate how the FDCA and FDA use these provisions to severely restrict drug manufacturers' ability to speak about off-label uses.<sup>27</sup> Subpart II.A.1 explores the new drug approval process, Subpart II.A.2 surveys the misbranding provisions of the FDCA, and, finally, Subpart II.A.3 examines the benefits and risks attendant to off-label use.

### 1. The New Drug Approval Process

Before 1962, drug manufacturers were not required to demonstrate that a new drug was safe or effective.<sup>28</sup> Rather, Congress required only that manufacturers' representations to physicians "be truthful and not misleading."<sup>29</sup> Harm resulting from false or misleading claims subjected manufacturers to criminal liability. However, due to the costs of litigation—financial and otherwise—ex post remedies proved utterly inadequate to deter manufacturers' misleading claims, especially in light of the potentially life threatening side-effects posed by some drugs.<sup>30</sup> Pre-1962, there was no adequate drug effectiveness testing, and physicians were inundated with obfuscatory promotional materials, making it nearly impossible for doctors to determine which drugs were safe and effective.<sup>31</sup> In 1962, Congress responded to these problems by amending the FDCA.<sup>32</sup>

25. See 21 U.S.C. § 352(n).

26. See *id.* § 333.

27. See generally Coleen Klasmeyer & Martin H. Redish, *Off-Label Prescription Advertising, the FDA and the First Amendment: A Study in the Values of Commercial Speech Protection*, 37 AM. J.L. & MED. 315 (2011).

28. Henry A. Waxman, *A History of Adverse Drug Experiences: Congress Had Ample Evidence to Support Restrictions on the Promotion of Prescription Drugs*, 58 FOOD & DRUG L.J. 299, 300–04 (2003).

29. *Id.* at 300.

30. *Id.* at 303. By the time there was sufficient evidence to support a finding that a drug was either unsafe or ineffective for a particular use, the public had often already suffered irreversible harm. See *id.* at 304–05. For example,

Mellaril, now a drug of last resort for schizophrenia because of its severe side effects—including sudden death—was widely promoted to general practitioners for . . . chronic fatigue, insomnia, anxiety, . . . apprehension, [and] vague digestive disorders . . .

. . . The severe risks associated with [Mellaril] could never justify [its] use for such minor conditions as everyday tension or insomnia, and yet that is exactly what [it was] promoted for in a setting where there was no effectiveness requirement for each promoted use.

*Id.* at 305 (citation omitted).

31. See *id.* at 303; see also S. REP. NO. 87-448, at 171, 204 (1961).

32. Waxman, *supra* note 28, at 300–06.

The Drug Amendments of 1962, still the centerpiece of the FDCA, require that all “new drug[s]” obtain FDA approval before being distributed in interstate commerce.<sup>33</sup> The approval process is threefold. First, a drug manufacturer must conduct a “series of pre-clinical and clinical trials.”<sup>34</sup> Second, a manufacturer must submit a report of its findings to the FDA along with a new drug approval application, by which it seeks to “demonstrate . . . that the drug . . . is both safe and effective for each of its intended uses.”<sup>35</sup> Third, the FDA reviews the submission, makes a determination as to whether the drug is safe and effective for its intended uses, and, depending on its conclusion, approves or denies the application.<sup>36</sup> If approved, the manufacturer is free, subject to further regulation, to sell and market its product.<sup>37</sup>

The FDCA defines a “new drug” as “[a]ny drug not generally recognized . . . as safe and effective for use under the conditions . . . suggested in the labeling thereof.”<sup>38</sup> “In the labeling thereof” dictates that, regardless of whether a drug has been approved for use in the treatment of *some* illness, it constitutes a “new drug” if *any* unapproved use is embodied in the drug’s labeling.<sup>39</sup> All “new drugs” must meet the FDCA’s approval requirements.<sup>40</sup> Thus, if a drug’s label embodies a use not approved by the

33. Drug Amendments of 1962, Pub. L. No. 87-781, § 104(a), 76 Stat. 780, 784 (codified as amended at 21 U.S.C. § 355(a) (2012)); *see also* 21 U.S.C. § 331(d); Waxman, *supra* note 28.

34. Wash. Legal Found. v. Friedman (*WLF I*), 13 F. Supp. 2d 51, 55 (D.D.C. 1998); *see also* 21 U.S.C. § 355(b)(1).

35. *WLF I*, 13 F. Supp. 2d at 55; 21 U.S.C. § 355(b)(1). FDA safety determinations do not conclusively establish that a drug is per se safe and effective. *See* Aaron S. Kesselheim, *Off-Label Drug Use and Promotion: Balancing Public Health Goals and Commercial Speech*, 37 AM. J.L. & MED. 225, 231–34 (2011). “The crux of the decision-making . . . is not simply whether the drug is efficacious or safe enough to be allowed on the market, but whether the drug’s efficacy and safety justify approval for a particular intended use.” *Id.* at 231. FDA determinations merely mean that a drug’s benefits outweigh its risks in the treatment of a particular illness for a particular class of patients. *Id.* at 232. For example, a drug that is effective in the treatment of both cancer and the common cold but significantly increases a patient’s likelihood of heart disease would not be approved by the FDA for treating the cold, but it may be approved by the FDA for treating cancer. Similarly, a drug that poses unreasonable risks to one class of patients would likely not be approved by the FDA for treatment of conditions within that class, but it may be approved by the FDA for treatment of another class to which the drug poses a lesser risk. *See id.* at 233–34.

36. *See* 21 U.S.C. § 355(d).

37. *Id.* § 331(d) (prohibiting “[t]he introduction or delivery for introduction into interstate commerce of any article in violation of section . . . 355”).

38. *Id.* § 321(p).

39. *Id.*

40. *Id.* § 355(a) (“No person shall introduce . . . into interstate commerce any new drug [without first obtaining] approval.”); Wash. Legal Found. v. Henney, 202 F.3d 331, 332 (D.C. Cir. 2000) (“[A drug] manufacturer must demonstrate that its product is safe and effective for each of its intended uses.”). A drug manufacturer avoids triggering the new drug approval process by conducting additional clinical trials and submitting a supplemental new drug application to the FDA. 21 C.F.R. § 314.70 (2013). The FDA then determines whether the new

FDA, a manufacturer may be held criminally liable for failing to obtain FDA approval for what, under the FDCA, constitutes a “new drug.”<sup>41</sup> Accordingly, a drug’s labeling is of great significance. Because the FDA’s definition of “label” is quite broad,<sup>42</sup> drug manufacturers are effectively prohibited from speaking about off-label uses in many instances, because “suggest[ing]” that a drug has any off-label use in those specified forms triggers the “new drug” requirements.<sup>43</sup>

## 2. Misbranding

The FDA seeks to control the flow of reliable, off-label information through the FDCA’s branding requirements. Once the FDA approves a drug, the drug’s labeling must comply with the FDCA’s branding requirements.<sup>44</sup> Failure to comply with the branding requirements subjects a manufacturer to criminal liability.<sup>45</sup> Under the FDCA, a drug is considered misbranded if its labeling lacks “adequate directions for use.”<sup>46</sup> “Adequate directions for use” are “directions under which the layman can use a drug safely and for the purposes for which it is intended.”<sup>47</sup> Because the FDCA expressly provides that a prescription drug is “not safe for use except under the supervision of a practitioner,”<sup>48</sup> under the FDCA, “it is impossible for a prescription drug’s labeling to contain adequate directions for use.”<sup>49</sup> Put another way, the FDCA mandates that drug manufacturers put directions on all drug labels (prescription and non-prescription) that a layperson can understand, but then asserts that in the case of prescription drugs there is no labeling a layperson can understand.<sup>50</sup> Thus, prescription drugs are per se misbranded.<sup>51</sup>

However, the FDCA also authorizes the FDA to “promulgate regulations exempting” drugs from the “adequate directions for use” requirement.<sup>52</sup>

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use is safe and effective for its additional intended uses. *See id.* § 314.2. If so, the use embodied on the label would no longer render the drug a “new drug” within the meaning of the act.

41. *See* 21 U.S.C. §§ 331(d), 355.

42. *Id.* § 321(m). The FDA defines labeling as “all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.” *Id.*

43. *See id.* § 355.

44. *Id.* § 352 (establishing requirements with which a drug’s label must comply to avoid being “misbranded”).

45. *Id.* §§ 331(a), 333(a).

46. *Id.* § 352(f).

47. 21 C.F.R. § 201.5 (2013); *see also* United States v. Articles of Drug, 625 F.2d 665, 672–73 (5th Cir. 1980) (validating the FDA’s interpretation of the FDCA).

48. 21 U.S.C. § 353(b)(1)(A).

49. *Articles of Drug*, 625 F.2d at 671.

50. *See id.*

51. *See id.*

52. 21 U.S.C. § 352(f).

Thus, the FDCA contemplates that the FDA will exempt prescription drugs from their per se misbranded status, and FDA regulations do exempt prescription drugs, subject to several conditions.<sup>53</sup> One such condition is that a prescription drug's labeling must "bear[] adequate information for its use, [such that] practitioners . . . [who can] administer the drug can use the drug safely and for the purposes for which it [was] intended, including all purposes for which it [was] advertised or represented."<sup>54</sup> By compelling a drug manufacturer to place on the labels of prescription drugs all of the uses for which it intends that a drug be prescribed, the FDA further restricts drug manufacturers' ability to speak about their drugs' off-label uses.<sup>55</sup> In effect, any drug manufacturer speech that could be construed as indicating an "objective intent" that one of its drugs be used off-label may subject that manufacturer to criminal liability.<sup>56</sup>

Prescription drug manufacturers must comply with the FDA's requirement that a drug's labeling bear "adequate information" for use by doctors. Failure to do so disqualifies the drug from the FDA's exemption, which is required in order to avoid being per se misbranded.<sup>57</sup> In satisfying the FDA's condition, a manufacturer that advertises or represents its product as being safe or effective for an off-label use must place on its drug's label information about that off-label use,<sup>58</sup> rendering the drug a "new drug," re-triggering the "new drug" approval requirements, and exposing the manufacturer to criminal liability.<sup>59</sup> These requirements, combined with the FDA's broad definition of "label" and the criminal sanctions attendant to a violation of the FDCA, severely limit drug manufacturers' ability to speak about off-label uses.<sup>60</sup>

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53. 21 C.F.R. § 201.100 (2013) (providing that a prescription "drug . . . shall be exempt from section [352(f)] if all the following conditions are met," and then proceeding to set forth a series of conditions); *see also* *Articles of Drug*, 625 F.2d at 674.

54. 21 C.F.R. § 201.100(c)(1); *see also* *id.* § 201.100(d)(1) (providing the same requirement for all other labeling).

55. *See* *United States v. Caputo*, 288 F. Supp. 2d 912, 920 (N.D. Ill. 2003) ("[T]he FDCA and the corresponding FDA regulations prohibit manufacturer promotion of off-label uses.").

56. The FDCA does not expressly prohibit drug manufacturers from speaking about off-label uses, but rather prohibits drug manufacturers from manifesting an objective intent that their products be used off-label. *See* *infra* Part IV.B. Evidence of such objective intent is primarily promotion, or speech.

57. *See* *supra* notes 44–51 and accompanying text.

58. *See* *supra* notes 54–55 and accompanying text.

59. *See* *supra* notes 39–41 and accompanying text.

60. *See* *Caputo*, 288 F. Supp. 2d at 920; *see also* 21 C.F.R. § 202.1(e)(4) (2013) ("An advertisement for a prescription drug . . . shall not recommend or suggest any use that is not in [its] labeling . . .").

### 3. Off-Label Use: Benefits & Risks

As mentioned, the FDA does not regulate the practice of medicine.<sup>61</sup> Thus, doctors are not prohibited from prescribing drugs off-label.<sup>62</sup> In fact, off-label prescribing is a relatively common practice in oncology, where few FDA-approved options often exist to treat patients faced with a high risk of mortality,<sup>63</sup> and in “pediatrics, where drug manufacturers are . . . reluctant to subject children to experimental clinical trials.”<sup>64</sup> Off-label use can be beneficial for the public,<sup>65</sup> and the FDA recognizes that in some areas of medicine, off-label use “constitute[s] the standard of good medical care.”<sup>66</sup> For example, Par Pharmaceuticals produces a prescription drug called Megace *ES* (“Megace”).<sup>67</sup> In July 2005, the FDA approved Megace for use in the treatment of “unexplained, significant weight loss in patients diagnosed with [AIDS]” known as “AIDS-related wasting.”<sup>68</sup> Physicians began prescribing Megace not only in the treatment of AIDS-related wasting, but also in the treatment of cancer-related wasting—an off-label use.<sup>69</sup> Megace is now so commonly prescribed for cancer-related wasting that, despite being an off-label use, it constitutes the standard of good medical care.<sup>70</sup>

In contrast, off-label prescribing can pose substantial risks, especially where there is little evidence of efficacy.<sup>71</sup> In the 1980s, for example, off-label prescribing of anti-arrhythmic drugs to treat heart attack patients doubled patients’ chances of mortality and led to the death of 3000 to

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61. 21 U.S.C. § 396 (2012) (“Nothing in this chapter shall be construed to . . . interfere with the authority of a [doctor] to prescribe . . . any legally marketed [product] for any condition or disease . . .”).

62. *Id.*

63. Kesselheim, *supra* note 35, at 235 (“Currently, off-label use of oncology drugs is encouraged as reasonable by the National Cancer Institute and in numerous publications, particularly for rare cancers where no treatment exist [sic] and in circumstances where high quality evidence exists despite no formal FDA approval.” (footnote omitted)). Some studies suggest that off-label prescribing is on the rise. *See id.* at 234–35 (comparing one study, which found that in 2001 there existed a “21% off-label prescription rate generally, and concluded that ‘[a]mong off-label mentions, most (73%) lacked evidence of clinical efficacy, and less than one-third (27%) were supported by strong scientific evidence,’” with another study conducted in 1985, which found that out of the top 1000 drugs prescribed by physicians, only thirty-one of those drugs were prescribed off-label (quoting David C. Radley et al., *Off-Label Prescribing Among Office-Based Physicians*, 166 ARCHIVES INTERNAL MED. 1021, 1023 (2006))).

64. *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51, 56 (D.D.C. 1998).

65. *Id.*

66. *Id.*

67. Par-Pharm Plaintiff’s Memorandum, *supra* note 3, at 10.

68. *Id.*

69. *Id.* at 10–11.

70. *Id.*; *see also* Jose Sierra, *The Morality of Off-Label Promotion*, PHARMARISC.COM (Mar. 19, 2012), <http://pharmarisc.com/2012/03/the-morality-of-off-label-promotion>.

71. *Cf.* Kesselheim, *supra* note 35, at 234–35 (discussing off-label concerns in oncology).

10,000 patients per year over a period of several years.<sup>72</sup> In those cases, a lack of available scientific evidence led to the prescription of drugs that proved harmful to patients.<sup>73</sup> Thus, off-label use is necessary to save lives in some cases where there are few available options that have proven effective, but the risks attendant to off-label use often outweigh the benefits. For this reason, the FDA is interested in controlling the flow of reliable, off-label information and in preventing drug manufacturers from circumventing the new drug approval process by getting drugs approved for one use, and then marketing those drugs for other, unapproved uses.

### B. THE COMMERCIAL SPEECH DOCTRINE

The Constitution mandates that “Congress shall make no law . . . abridging the freedom of speech.”<sup>74</sup> Under the First Amendment, different forms of speech are afforded different levels of protection.<sup>75</sup> “[T]he First Amendment imposes tight constraints upon government efforts to restrict . . . ‘core’ political speech.”<sup>76</sup> In contrast, commercial speech, or speech which does no more “than propos[e] a commercial transaction,” is afforded lesser First Amendment protection.<sup>77</sup> In fact, until the mid-1970s, commercial speech was afforded no First Amendment protection whatsoever.<sup>78</sup> Drug manufacturer speech, even that which is to some degree educational or scientific, is commercial speech.<sup>79</sup>

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72. *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51, 56 (D.D.C. 1998).

73. *See id.* Whether the benefits associated with off-label prescribing outweigh the risks is outside of the scope of this Note. This Note is only concerned with the First Amendment as it relates to the FDA’s off-label speech restrictions. For a thorough discussion concerning the current FDA drug regulatory system, see A. Devesh Tiwary, *Off-Label Use of Prescription Drugs Should Be Regulated by the FDA (2003)* (unpublished third year paper) (on file with Harvard Law School), available at <http://dash.harvard.edu/handle/1/8852151> (follow hyperlink to download PDF).

74. U.S. CONST. amend. I.

75. *See Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2674 (2011) (Breyer, J., dissenting). In *Washington Legal Foundation v. Friedman*, the court concluded that the speech was commercial because: (1) it was an advertisement, in that it “call[ed] public attention to . . . [the] desirable qualities [of the product] so as to arouse a desire to buy”; (2) it made reference to a specific product; and (3) it was made by a speaker who had “an economic motivation.” *WLF I*, 13 F. Supp. 2d at 64 (internal quotation marks omitted); *see also* *United States v. Caronia*, 703 F.3d 149, 163 (2d Cir. 2012).

76. *Sorrell*, 131 S. Ct. at 2673 (Breyer, J., dissenting).

77. *Id.* at 2674 (quoting *Ohralik v. Ohio State Bar Ass’n*, 436 U.S. 447, 455–56 (1978)).

78. *See Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 776 (1976) (Stewart, J., concurring) (“[T]he Constitution imposes no such restraint on government as respects purely commercial advertising.’ For more than 30 years this ‘casual, almost offhand’ statement in *Chrestensen* has operated to exclude commercial speech from the protection afforded by the First Amendment to other types of communication.” (citations omitted)).

79. *See Bolger v. Youngs Drug Prods. Corp.*, 463 U.S. 60, 67–68 (1983).

This Subpart discusses the development of the commercial speech doctrine. Subpart II.B.1 details the commercial speech analysis established by *Central Hudson Gas & Electric Corp. v. Public Service Commission of New York*. It then discusses *Thompson v. Western States Medical*, a more recent case that demonstrates how the modern Court applies *Central Hudson*. Subpart II.B.2 explains *Sorrell v. IMS Health Inc.*, a recent case that raises the question of whether courts should apply strict scrutiny when analyzing the constitutionality of off-label speech restrictions.

1. *Central Hudson and Thompson v. Western States Medical*

In 1976, the Supreme Court held for the first time, in *Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, that commercial speech is entitled to First Amendment protection.<sup>80</sup> In striking down a Virginia statute banning the advertisement of drug prices, the Court made clear that its holding did not extend so far as to limit the government's ability to regulate all commercial speech, leaving open the question of when government restrictions on commercial speech are permissible.<sup>81</sup> The Court answered that question in *Central Hudson* when it struck down a state regulation banning utility companies from advertising their services.<sup>82</sup> The Court developed and applied a three-prong intermediate scrutiny test to determine that the First Amendment precluded the government from regulating particular commercial speech.<sup>83</sup> *Central Hudson's* intermediate scrutiny test requires that the speech "must concern lawful activity and not be misleading,"<sup>84</sup> as the First Amendment does not protect unlawful or misleading speech.<sup>85</sup> If the speech is lawful and not misleading, then the government must show: (1) it has a "substantial interest" in regulating the speech; (2) the "regulation 'directly advances' that interest"; and (3) the restriction "is 'not more extensive than is necessary' to serve the interest."<sup>86</sup> The government bears the burden of proving these three elements.<sup>87</sup>

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80. See *Va. State Bd.*, 425 U.S. at 776 (Stewart, J., concurring).

81. *Id.* at 770–71 (majority opinion).

82. *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557, 558, 561 (1980).

83. *Id.* at 566; Garner & Whitney, *supra* note 14, at 492–93 n.67.

84. *Cent. Hudson*, 447 U.S. at 566.

85. *Id.* at 563.

86. *Id.* at 591 (Rehnquist, J., dissenting); Garner & Whitney, *supra* note 14, at 492.

87. See *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 373 (2002) ("[I]t is well established that 'the party seeking to uphold a restriction on commercial speech carries the burden of justifying it.'" (quoting *Edenfield v. Fane*, 507 U.S. 761, 770 (1993))). In applying the test, the Court in *Central Hudson* concluded that the State had a substantial interest in ensuring that utility rates were "fair and efficient," and that the ban on speech directly advanced that interest. *Cent. Hudson*, 447 U.S. at 569. However, the Court concluded that the outright ban on speech was "more extensive than is necessary." *Id.* at 572. First, the Court considered the fact that the ban actually prohibited speech made by utility companies that

The *Central Hudson* framework remains the standard by which the modern Court adjudges commercial speech regulations.<sup>88</sup> In 2002, the Supreme Court in *Thompson* struck down an advertising ban on pharmacies of compounded drugs using *Central Hudson*'s third prong.<sup>89</sup> The government did not argue the banned advertising was unlawful or misleading such that the First Amendment did not protect the advertising. Rather, the government argued that its ban satisfied *Central Hudson*'s requirements.<sup>90</sup> The Court held the government has a "substantial interest" in "[p]reserving the effectiveness and integrity of the . . . new drug approval process" and "in permitting the continuation of the practice of compounding so that patients with particular needs [can] obtain medications suited to those needs."<sup>91</sup> The Court assumed the government's advertising ban "directly advanced" that interest. However, in weighing the third prong, the Court reasoned that because the Court itself could identify less restrictive means of achieving those ends, the government's ban was unduly restrictive.<sup>92</sup> The Court emphasized that the government "carrie[d] the burden of justifying it[s] ban,]" and because the government could not explain why non-speech-restrictive alternatives "alone or in combination" would not suffice, the regulations were unconstitutional under *Central Hudson*'s third prong.<sup>93</sup> Thus, today, *Central Hudson* imposes a heavy burden on the government.

## 2. *Sorrell v. IMS Health*: A Game Changer?

*Sorrell v. IMS Health Inc.* also addressed drug manufacturer speech and has generated considerable debate concerning the standard of scrutiny applicable to the FDA's off-label speech restrictions. The confusion surrounding *Sorrell*'s impact on the level of scrutiny stems from the *Sorrell* Court's use of the terms "content-based restrictions" and "speaker-based restrictions," as well as intimations that all laws that burden particular

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would encourage consumption of more efficient recourses, which would actually advance the State's asserted interest; thus, the regulation was unjustifiably over-inclusive. *Id.* at 568–71. Second, the Court noted that the State had failed to establish that less restrictive alternatives would not suffice, such as restricting "the format and content of . . . advertising," or compelling the disclosure of "relative efficiency and expense" of information. *Id.* at 571.

88. See, e.g., *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2667–68 (2011) (applying the *Central Hudson* framework); *Thompson*, 535 U.S. at 367 (same); 44 *Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 504 (1996) (same).

89. *Thompson*, 535 U.S. at 371. Compounded drugs are those whose ingredients are tailored to the needs of individual patients. Compounded drugs are exempted from having to obtain FDA approval, as compounding is beneficial to patients with unique prescription needs. *Id.* at 360–61.

90. *Id.* at 370.

91. *Id.* at 369.

92. *Id.* at 372–73. The Court noted several less speech-restrictive alternatives, including banning "commercial scale manufacturing . . . equipment for compounding." *Id.* (internal quotation marks omitted).

93. *Id.* at 373.

content and speakers are subject to strict scrutiny, coupled with its express assertions that there are cases in which content- and speaker-based restrictions need only pass *Central Hudson's* less-exacting intermediate scrutiny.<sup>94</sup> Ultimately, the Court in *Sorrell* did not decide whether the challenged law was subject to strict scrutiny, as the Court found the Vermont law failed even *Central Hudson's* intermediate scrutiny.<sup>95</sup> However, this left unresolved a disconcerting question: Why might strict scrutiny apply in a case that seemed to be clearly governed by *Central Hudson*?<sup>96</sup>

a. *Vermont's Act*

*Sorrell* concerned a challenge to a Vermont Act (the “Act”) that banned data miners from selling physician prescription data to drug manufacturers for use in marketing and prohibited drug manufacturers from using physician prescription data for marketing purposes.<sup>97</sup> The Act expressly authorized the sale of physician prescription data for use in non-marketing related endeavors, including “health care research” and physician education.<sup>98</sup> The Act also created a drug-education program, which was expressly designed to “counter-detail,” or to persuade doctors to prescribe generic drugs.<sup>99</sup> Counter-detailers could use physician prescription data, whereas detailers could not.<sup>100</sup> Legislative findings accompanying the Act showed that the Vermont legislature determined that the aims of brand-name drug manufacturers’ marketing programs, specifically detailing, often clash with the state’s objectives, and that the “marketplace for ideas” as it relates to prescription drug safety and efficacy is frequently asymmetrical and causes doctors to make decisions based on “incomplete and biased

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94. *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2677 (2011) (Breyer, J., dissenting) (“The Court (suggesting a standard yet stricter than *Central Hudson*) says that we must give content-based restrictions that burden speech ‘heightened’ scrutiny. It adds that ‘[c]ommercial speech is no exception.’ And the Court then emphasizes that this is a case involving both ‘content-based’ and ‘speaker-based’ restrictions. But neither of these categories—‘content-based’ nor ‘speaker-based’—has ever before justified greater scrutiny when regulatory activity affects commercial speech.” (citations omitted)).

95. *Id.* at 2659 (majority opinion).

96. *Cf. id.* at 2678 (Breyer, J., dissenting) (“If the Court means to create constitutional barriers to regulatory rules that might affect the *content* of a commercial message, it has embarked upon an unprecedented task . . .”).

97. *Id.* at 2660 (majority opinion); *see also* VT. STAT. ANN., tit. 18, § 4631 (2009), *declared unconstitutional by Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653 (2011). Data miners are companies that buy physician prescription data from pharmacies and insurance companies. *Sorrell*, 131 S. Ct. at 2660. Brand name drug manufacturers use physician prescription data to tailor their representatives’ messages to fit physician prescribing practices and to target physicians who are most likely to prescribe their drugs—a practice typically referred to as detailing. *Id.* at 2659. Detailing is an expensive process and typically proves unprofitable once a drug’s patent expires and generics enter the market. *Id.* at 2660.

98. *Sorrell*, 131 S. Ct. at 2660–61 (quoting VT. STAT. ANN., tit. 18, § 4631(e) (2007)).

99. *Id.* at 2661.

100. *Id.*

information.”<sup>101</sup> The Act also contained an “opt-out” provision allowing physicians to consent to manufacturers’ use of their data.<sup>102</sup>

In addressing whether the Act violated the First Amendment, the Supreme Court first discussed why the Act may be subject to strict scrutiny before ultimately striking it down under *Central Hudson’s* less-exacting, intermediate scrutiny framework.

*b. Strict Scrutiny: Evidence of Viewpoint Discrimination*

The *Sorrell* Court’s discussion of strict scrutiny began with the premise that it is typically “dispositive to conclude that a law is . . . viewpoint-discriminatory,” as such laws are subject to strict scrutiny and are highly suspect.<sup>103</sup> The Court noted several factors indicating that the Act was viewpoint discriminatory.<sup>104</sup> First, the Court noted that the Act burdened particular content (marketing) and particular speakers (drug manufacturers.)<sup>105</sup> The Court viewed this as evidence that the Act was intended to suppress a disfavored point of view, as laws that burden particular content and speakers necessarily elevate unburdened viewpoints.<sup>106</sup> Second, the Court considered Vermont’s legislative findings, which explicitly asserted that the purpose of the Act was to render drug manufacturers’ marketing efforts ineffective because they were too persuasive and conflicted with Vermont’s counter-detailing efforts.<sup>107</sup> Though the Court found these factors pointed toward the Act being viewpoint discriminatory, the Court did not definitively conclude that the Act was viewpoint discriminatory or that strict scrutiny applied. Rather, the Court found the Act failed even *Central Hudson’s* intermediate scrutiny analysis.<sup>108</sup>

*c. Intermediate Scrutiny*

A conclusion that Vermont’s Act was viewpoint discriminatory would have been dispositive. However, the Court failed to formally find that the Act was viewpoint discriminatory and proceeded instead to apply *Central*

101. *Id.* (internal quotation marks omitted).

102. *See id.* at 2660.

103. *Id.* at 2667; *see also id.* at 2664 (“The First Amendment requires heightened scrutiny whenever the government creates ‘a regulation of speech because of disagreement with the message it conveys.’” (quoting *Ward v. Rock Against Racism*, 491 U.S. 781, 791 (1989))).

104. *Id.* at 2663–65.

105. *Id.* at 2663.

106. *See id.* (“‘In its practical operation,’ Vermont’s law ‘goes even beyond mere content discrimination, to actual viewpoint discrimination.’” (quoting *R.A.V. v. St. Paul*, 505 U.S. 377, 391 (1992))).

107. *Id.* at 2663–64.

108. *Id.* at 2667–68.

*Hudson's* intermediate scrutiny test.<sup>109</sup> The Court noted that content- or speaker-based commercial regulations burdening speech are justifiable upon a showing of identifiable commercial harm attendant to the restricted speech.<sup>110</sup> Vermont suggested several harms that accompany drug manufacturers' marketing efforts.<sup>111</sup> However, the Court found, through its application of *Central Hudson*, that the Act did not counteract those harms, nor did Vermont show that such harms were actually present.<sup>112</sup> Thus, Vermont's justifications seemed to be mere pretext.<sup>113</sup>

First, Vermont argued that doctors and patients have a right to medical privacy and have a reasonable expectation that the recording of prescriptions will be used only for "filling and processing" purposes.<sup>114</sup> The Court demonstrated that if the Act was designed to protect privacy, it was perplexingly underinclusive because it made doctor-prescription data "available to an almost limitless audience."<sup>115</sup> Thus, unless drug manufacturers were shown to pose unique privacy harms, the law did not appear to counteract privacy concerns.<sup>116</sup> Vermont offered a few instances where doctors claimed they were subjected to harassing sales techniques in an attempt to demonstrate unique privacy harms stemming from drug manufacturers' use of detailing information, but the Court was unwilling to accept such anecdotal evidence as the basis for such a sweeping restriction.<sup>117</sup> Given the Act's inherent ineffectiveness at counteracting privacy concerns, and an absence of evidence demonstrating unique privacy harms resulting from drug manufacturers' use of prescribing data, the "privacy" justification seemed a pretext.<sup>118</sup>

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109. *See id.* at 2667 ("In the ordinary case it is all but dispositive to conclude that a law is content-based and, in practice, viewpoint-discriminatory. . . . As in previous cases, however, the outcome is the same whether a special commercial speech inquiry or a stricter form of judicial scrutiny is applied.").

110. *See id.* at 2672 (holding that upon a showing of some likelihood of commercial harm, "content-based restrictions on protected expression are . . . permissible . . . . [H]owever, Vermont has not shown that its law has [such a] justification").

111. *Id.* at 2668.

112. *See id.* at 2668-72.

113. *See id.* at 2669 ("The limited range of available privacy options instead reflects the State's impermissible purpose to burden disfavored speech.").

114. *Id.* at 2668 (internal quotation marks omitted).

115. *Id.* (considering that "the State could have addressed physician confidentiality through 'a more coherent policy.'" (quoting *Greater New Orleans Broad. Ass'n v. United States*, 527 U.S. 173, 195 (1999))).

116. *See id.* at 2669.

117. *See id.* at 2669-70.

118. *See id.* at 2669 ("Rules that burden protected expression may not be sustained when the options provided by the State are too narrow to advance legitimate interests or too broad to protect speech. As already explained, [the Act] permits extensive use of prescriber-identifying information and so does not advance the State's asserted interest in physician confidentiality. The limited range of available privacy options instead reflects the State's impermissible purpose to burden disfavored speech.").

Second, Vermont argued that the law was enacted to promote the public health by reducing drug prices for consumers.<sup>119</sup> Vermont asserted that the law achieved this end by reducing the effectiveness of manufacturers' detailing efforts, which would in turn increase generic-drug prescribing rates.<sup>120</sup> The Court found the Act did not seem to actually promote that goal.<sup>121</sup> First, in many cases, brand-name drugs may be the only available option, especially given the fact that detailing is an expensive tactic that generally proves unprofitable once a drug is no longer protected by patent and generics enter the market.<sup>122</sup> Thus, the regulation would likely have little impact on price.<sup>123</sup> Second, the law's opt-out policy allowed physicians to provide drug manufacturers access to their information.<sup>124</sup> Given evidence that many doctors found detailing to be helpful, some doctors would likely opt out, and brand-name prescribing rates would not be significantly affected.<sup>125</sup> Moreover, if the Act were truly intended to counteract high drug prices, it would not have logically contained a mechanism through which decisions made by independent actors could render it wholly ineffective.<sup>126</sup> The Act's ineffectiveness evinced the pretextual nature of this justification, which buttressed the Court's view that the Act was viewpoint discriminatory.<sup>127</sup>

Vermont's second justification was more problematic because, if the purpose of the Act was to reduce drug prices for consumers, the Act sought to do so by impermissibly controlling the flow of factual information based on a "fear that people would make bad decisions if given truthful information."<sup>128</sup> As the Court noted:

Vermont may be displeased that detailers who use prescriber-identifying information are effective in promoting brand-name drugs. The State can express that view through its own speech. But a State's failure to persuade does not allow it to hamstring the opposition. The State may not burden the speech of others in order to tilt public debate in a preferred direction. . . . [T]he

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119. *Id.* at 2670.

120. *Id.*

121. *Id.* ("[T]he 'state's own explanation of how' [the Act] 'advances its interests cannot be said to be direct.'").

122. *Id.*

123. *See id.*

124. *Id.* at 2660.

125. *See id.* at 2670 ("If pharmaceutical marketing affects treatment decisions, it does so because doctors find it persuasive.").

126. *Cf. id.*

127. *Id.*

128. *Id.* at 2670–71 (quoting *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 374 (2002)) (internal quotation marks omitted).

general rule is that the . . . audience, not the government, assess the value of the information presented.<sup>129</sup>

The content- or speaker-based restrictive nature of the Act, the legislative history of the Act, the education provisions enacted to counter-detail, the ineffectiveness of the Act in achieving Vermont's asserted objectives, and the impermissible way in which the Act achieved its latter objective all support the conclusions that the Act was objectively viewpoint discriminatory and that the Act was in violation of the rule of *Central Hudson* and therefore the First Amendment.<sup>130</sup>

### III. FIRST AMENDMENT CHALLENGES TO THE FDA'S OFF-LABEL SPEECH RESTRICTIONS

Prior to *United States v. Caronia*,<sup>131</sup> two cases addressed the FDA's authority to regulate off-label speech: *Washington Legal Foundation v. Friedman*<sup>132</sup> and *United States v. Caputo*.<sup>133</sup> This Part discusses these three cases in order to demonstrate how courts' analyses of First Amendment challenges to the FDA's off-label speech restrictions differ following *Sorrell*.

#### A. WASHINGTON LEGAL FOUNDATION V. FRIEDMAN

The plaintiffs<sup>134</sup> in *Washington Legal Foundation v. Friedman* ("WLF I") did not challenge the FDA's off-label restrictions in their entirety. They only challenged FDA guidance documents restricting drug manufacturers' ability to sponsor Continuing Medical Education seminars ("CMEs") and disseminate peer-reviewed, medical-journal articles to physicians.<sup>135</sup> The WLF I challenge was a narrow challenge to the specific restrictions embodied in the guidance documents.<sup>136</sup> Where CMEs and medical journals addressed off-label uses, the FDA's guidance documents sought to delineate the point at which drug manufacturers' sponsorship or influence amounted to an "objective intent" to promote off-label uses in violation of the FDA's

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129. *Id.* at 2671–72 (citations omitted) (internal quotation marks omitted).

130. *See generally Sorrell*, 131 S. Ct. 2653.

131. *See infra* Part III.C.

132. *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51, 52 (D.D.C. 1998).

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

134. The plaintiffs in *WLF I* were "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'" called the Washington Legal Foundation. *WLF I*, 13 F. Supp. 2d at 54.

135. *Id.* Over the years, the FDA has drafted and distributed guidance documents to address new and evolving issues. CMEs are comprised of seminars and symposia that often address a wide variety of topics, some of which seek to educate doctors about the risks and benefits associated with both on-label and off-label uses of particular drugs. *See id.* at 57–58.

136. *Id.* at 54.

restrictions, and thereby the FDCA.<sup>137</sup> The plaintiffs in *WLF I* challenged where the FDA had drawn this line, arguing it violated drug manufacturers' First Amendment rights.<sup>138</sup> Applying *Central Hudson*, the *WLF I* court held that the FDA's guidance document restrictions were unconstitutional.<sup>139</sup>

The court first concluded that the First Amendment protected the regulated, off-label speech at issue because it was lawful and not misleading.<sup>140</sup> As to the legality of the speech, the court noted that the proper question is "whether the conduct that the speech promotes violates the law."<sup>141</sup> Because the speech in question promoted off-label use, and off-label use is lawful, the court concluded that the speech was lawful.<sup>142</sup> As to whether the speech was misleading, the court considered whether the speech was "inherently misleading" by looking for "possibilities for deception," "experience . . . prov[ing] that . . . such advertising is subject to abuse," and "the ability of the intended audience to evaluate the claims made."<sup>143</sup> The court noted that the FDA did not restrict the dissemination of similar information by all persons, but only restricted dissemination by drug manufacturers.<sup>144</sup> The court found that information itself could not be misleading merely as a result of who presented it.<sup>145</sup> Moreover, the court noted that because physicians are a highly educated, sophisticated audience, they were unlikely to be misled by the information.<sup>146</sup> Given these factors, the court concluded that the speech was not inherently misleading. Thus, the government bore the burden of justifying the regulation under *Central Hudson*'s three prongs.<sup>147</sup>

Under *Central Hudson*'s first prong, the FDA argued it had two "substantial interests" in regulating the challenged speech: (1) "ensuring that physicians receive accurate and unbiased information so that they [could] make informed prescription choices"; and (2) preventing drug

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137. The FDA used a twelve-factor test it considered to draw the line between promotion and non-promotion. Guidance for Industry: Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64,093, 64,096-99 (Dec. 3, 1997). At that time, the FDA interpreted guidance documents as legally binding, meaning the FDA's position was that a violation of the rules set forth in the guidance documents constituted a violation of FDA regulations, and thus the FDCA. This is no longer the case, as today guidance documents are viewed as merely guidance. *Id.* at 64,094 n.1.

138. *WLF I*, 13 F. Supp. 2d at 54.

139. *Id.* at 72-74.

140. *Id.* at 69.

141. *Id.* at 66.

142. *Id.* The FDA argued that a drug is "misbranded as a matter of law" where the manufacturer promotes off-label use of the drug. *Id.* The court rejected this circular reasoning, noting that "the tautological nature of this argument exposes its shortcomings." *Id.*

143. *Id.* at 66-67 (citations omitted) (internal quotation marks omitted).

144. *Id.* at 67.

145. *Id.*

146. *Id.* at 70.

147. *Id.* at 69-74.

manufacturers from circumventing the new drug approval process by obtaining FDA approval for one use and promoting their products for unapproved, off-label uses.<sup>148</sup> The court rejected the first justification as “wholly and completely unsupportable” and in conflict with Supreme Court decisions holding that “a State’s paternalistic assumption that the public will use truthful, nonmisleading . . . information unwisely” if made available to it constituted insufficient justification for speech restrictions.<sup>149</sup> Furthermore, the FDA’s interest in ensuring receipt of unbiased, accurate information was minimized given the evaluative skills of physicians.<sup>150</sup> The court, however, accepted the FDA’s second justification, that the FDA has a substantial interest in preventing drug manufacturers from circumventing the new drug approval process.<sup>151</sup>

Applying the second prong, the court concluded that the FDA’s substantial interest was “directly advance[d]” through its suppression of off-label speech.<sup>152</sup> In so concluding, the court found that manufacturer promotional efforts in fact increase off-label prescribing. Additionally, the court found high costs associated with getting off-label uses on-label—coupled with drug manufacturer uncertainty about whether subsequent clinical trials would prove effective and whether obtaining additional off-label indications would allow manufacturers to fully recoup clinical trial costs—created substantial disincentives for drug manufactures to get off-label uses on-label.<sup>153</sup> Thus, given the effectiveness of off-label promotional techniques, and the disincentives attendant to getting off-label uses on-label, the court concluded that the FDA’s interest was directly advanced in limiting drug manufacturers’ ability to take advantage of effective promotional techniques.<sup>154</sup>

However, the court found that the FDA’s speech restrictions were nevertheless unconstitutional under *Central Hudson’s* third prong because they were “considerably more extensive than necessary,” and the FDA had not explained why less speech-restrictive means would not suffice.<sup>155</sup> The court reasoned that “full disclosure” was a less restrictive and equally effective means to incentivize drug manufacturers to get off-label uses on-label.<sup>156</sup> Full disclosure would make doctors aware of the off-label nature of

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148. *Id.* at 69–71.

149. *Id.* at 69–70 (quoting 44 *Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 497 (1996)) (internal quotation marks omitted).

150. *Id.* at 70.

151. *Id.* at 70–71. Put another way, the FDA alleged, and the court agreed, that the FDA had an interest in incentivizing drug manufacturers “to get off-label uses on-label.” *Id.* at 70.

152. *Id.* at 72.

153. *Id.*

154. *Id.*

155. *Id.* at 73.

156. *Id.*

the promotions, and since doctors are presumably less inclined to prescribe drugs off-label, drug manufacturers would continue to seek the FDA's approval.<sup>157</sup> Because the plaintiffs in *WLF I* only challenged the FDA's guidance documents—not the FDA's speech restrictions in their entirety—the court concluded that adequate incentives, including restrictions on all other promotional speech, remained to compel manufacturers to get off-label uses on-label.<sup>158</sup> The court then declared the guidance documents unconstitutional.<sup>159</sup>

#### B. UNITED STATES V. CAPUTO

*United States v. Caputo* involved the criminal prosecution of several AbTox, Inc. corporate officers who were indicted for promoting non-FDA approved uses of their products.<sup>160</sup> The defendants argued that the FDA's off-label speech restrictions violated their First Amendment rights.<sup>161</sup> *Caputo* differed from *WLF I* in that the defendants in *Caputo* challenged the FDA's restrictions in their entirety.<sup>162</sup> As in *WLF I*, the court applied *Central Hudson's* commercial speech analysis and deferred to the *WLF I* court's analysis in applying the first two prongs of *Central Hudson*.<sup>163</sup> However, applying the third prong, the court found that, unlike *WLF I*, the *Caputo* “[d]efendants’ First Amendment challenge [struck] at the very heart of the

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157. *Id.*

158. *Id.* at 72.

159. *Id.* at 74. Following the district court's decision in *WLF I*, Congress enacted the Food and Drug Administration Modernization Act of 1997 (“FDAMA”), which adopted some of the policies previously embodied in the FDA's guidance documents and partially in conflict with *WLF I*. See Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (codified as amended at 21 U.S.C. §§ 301–394 (2012)). The plaintiffs from *WLF I* challenged the regulations again and the court extended its previous ruling to apply to the FDAMA. See *Wash. Legal Found. v. Henney (WLF II)*, 56 F. Supp. 2d 81, 84 (D.D.C. 1999), *vacated in part*, 202 F.3d 331 (D.C. Cir. 2000). The FDA appealed the decision to the D.C. Circuit Court of Appeals, changing its position and arguing for the first time that neither the FDAMA nor the guidance documents independently authorized the FDA to regulate off-label speech, but rather merely created “safe harbors.” *Wash. Legal Found. v. Henney*, 202 F.3d 331, 335 (D.C. Cir. 2000). Compliance with the conditions in the safe harbor provisions immunized drug manufacturers from misbranding actions. *Id.* The appellate court accepted this interpretation, and as a result the controversy “disappeared,” as the challenged restrictions no longer negatively impacted drug manufacturers, and the plaintiffs had not challenged the FDA's broader restrictions. *Id.* The district court's decision was accordingly vacated. *Id.* at 337. This procedural technicality allowed the FDA to avoid what may have otherwise resulted in a pro-First Amendment D.C. Circuit Court decision.

160. *United States v. Caputo*, 288 F. Supp. 2d 912, 914–16 (N.D. Ill. 2003). Medical devices are governed by the same regulations as are prescription drugs, and thus manufacturers of medical devices are likewise prohibited from promoting their products for non-FDA approved uses. See *id.* at 919.

161. *Id.* at 918–19.

162. *Id.* at 919.

163. *Id.* at 920–21.

FDA's ability to proscribe manufacturer promotion of off-label uses."<sup>164</sup> Because the court was unable to identify less speech-restrictive alternatives, it concluded that the FDA's regulations were "not more extensive than necessary," and thus constitutional.<sup>165</sup>

### C. UNITED STATES V. CARONIA

*United States v. Caronia* is the first and, thus far, only off-label case decided after *Sorrell*.<sup>166</sup> *Caronia* demonstrates one possible interpretation of *Sorrell* as requiring courts to assess off-label speech restrictions under a more heightened form of scrutiny than the *Central Hudson* test.<sup>167</sup> *Caronia* was convicted of having criminally misbranded a drug.<sup>168</sup> *Caronia* was hired by Orphan Medical as a pharmaceutical sales representative to promote its product, Xyrem; Orphan Medical educated him on Xyrem's available off-label uses but did not encourage him to promote off-label—at least not explicitly.<sup>169</sup> He then spoke with physicians about the off-label uses of Xyrem and told them "how to hide . . . off-label [prescribing practices] for billing purposes in order to avoid reimbursement issues."<sup>170</sup>

One such physician was an FDA informant.<sup>171</sup> The FDA used taped conversations to prove that *Caronia* intended to distribute a misbranded drug in interstate commerce.<sup>172</sup> *Caronia* argued that the use of such evidence, namely his speech, violated his First Amendment rights.<sup>173</sup>

The Second Circuit majority, in a 2-1 decision, held "that the government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label

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164. *Id.* at 922.

165. *Id.* On appeal, the Seventh Circuit did not reach the constitutional question because the jury found one of the products promoted by defendants had never obtained the FDA's approval for any use. *United States v. Caputo*, 517 F.3d 935, 940 (7th Cir. 2008). Thus, because the product itself could not have been sold lawfully, the convictions would stand regardless of whether the defendant's First Amendment challenge was successful. *Id.* Accordingly, the court did not reach the First Amendment issue and affirmed the lower court's decision. *Id.* at 944.

166. See Alison Frankel, *Why U.S. Is Forgoing Appeal of Landmark 2nd Circuit Off-Label Ruling*, REUTERS (Jan. 24, 2013), <http://blogs.reuters.com/alison-frankel/2013/01/24/why-u-s-is-forgoing-appeal-of-landmark-2nd-circuit-off-label-ruling>.

167. See Sierra, *supra* note 11.

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

169. *Id.* at 155-56.

170. Jose Sierra, *Government's Hammer Lands on GSK; Industry Warned*, PHARMARISC.COM (July 9, 2012), <http://pharmarisc.com/2012/07/governments-hammer-lands-on-gsk-industry-warned>.

171. *Caronia*, 703 F.3d at 156.

172. *Id.* at 156-57.

173. *Id.* at 158, 160. *Caronia* presents an interesting case because, under the current regulatory regime, the defendant was free to discuss Xyrem in his capacity as a doctor, but not in his capacity as a representative for Orphan Medical.

use of an FDA-approved drug.”<sup>174</sup> The FDA argued that its “objective intent” provisions did not outright prohibit drug manufacturers or their affiliates from promoting off-label uses.<sup>175</sup> Instead, the provisions merely allowed the government to use speech as evidence of drug manufacturers’ intent that their products be used off-label.<sup>176</sup> While the Second Circuit recognized that the FDA does “not expressly prohibit . . . off-label promotion,” the court ultimately rejected the FDA’s argument, noting that the defendant was being prosecuted for his speech, as his speech was the only evidence of his intent.<sup>177</sup>

Having concluded that the FDA was prosecuting the defendant for his speech, the court considered whether the First Amendment protected the speech.<sup>178</sup> First, the court considered whether it would apply some form of strict scrutiny, pursuant to *Sorrell*, or intermediate scrutiny, pursuant to *Central Hudson*.<sup>179</sup> The court noted that, as in *Sorrell*, the FDA’s regulations were “content-based because [they] distinguish[ed] between ‘favored speech’ and ‘disfavored speech on the basis of the ideas or views expressed.’”<sup>180</sup> The court also noted that, as in *Sorrell*, the FDA’s regulations were speaker-based because they applied to drug manufacturers, and only drug manufacturers.<sup>181</sup> Given the content- and speaker-based nature of the restrictions, the court concluded that, under *Sorrell*, some form of heightened scrutiny beyond that of *Central Hudson* was necessary.<sup>182</sup> However, the court did not have occasion to apply such heightened scrutiny—strict scrutiny or otherwise—because the court found the FDA’s off-label speech restrictions failed even *Central Hudson*’s intermediate scrutiny.<sup>183</sup>

Applying *Central Hudson*, the court concluded that the first prong was “easily satisfied,” as the government has a substantial interest in drug safety, public health, and in preserving the integrity of the new drug approval process to reduce patient exposure to unsafe and ineffective drugs.<sup>184</sup> The court then concluded that the FDA’s speech restrictions did not satisfy *Central Hudson*’s second prong, holding that the restrictions did not “directly

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174. *Id.* at 169.

175. *See id.* at 154.

176. *Id.* at 155.

177. *Id.* at 160, 162.

178. *Id.* at 162–63.

179. *Id.* at 163–64.

180. *Id.* at 165. FDA-approved speech was permitted whereas unapproved speech was restricted.

181. *Id.*

182. *Id.*

183. *Id.* at 164.

184. *Id.* at 165–66.

advance” that interest.<sup>185</sup> The court reasoned that because doctors are capable of prescribing drugs off-label, restricting “the truthful promotion of off-label drug usage” does not “directly . . . reduc[e] patient exposure to unsafe and ineffective drugs.”<sup>186</sup>

Under the final prong, the court concluded the FDA’s off-label promotion restrictions were not narrowly drawn to further the FDA’s interests.<sup>187</sup> Citing *Thompson*, the court noted that the government could employ several less restrictive alternatives to achieve its interests.<sup>188</sup> The court concluded that because the FDA could not explain why plausible alternatives would not suffice, the FDA had failed *Central Hudson*’s final prong.<sup>189</sup> Accordingly, as the FDA’s restrictions failed both *Central Hudson*’s second and third prongs, the FDA’s prosecution of a manufacturer for speech promoting the lawful, off-label use of an FDA-approved drug was unconstitutional.<sup>190</sup>

#### IV. ANALYSIS & SOLUTION

Courts addressing the constitutionality of the FDA’s off-label speech restrictions should not interpret *Sorrell* to stand for the proposition that the FDA’s restrictions are subject to strict scrutiny or another form of heightened scrutiny. Rather, courts should continue to assess the FDA’s restrictions under *Central Hudson*’s intermediate scrutiny. However, regardless of whether the government’s off-label speech restrictions are subject to strict or intermediate scrutiny, FDA speech regulations are likely unconstitutional under *Central Hudson*. Accordingly, Congress and the FDA must act to bring the current law into conformity with the First Amendment.

Subpart IV.A discusses *Sorrell*’s import in the off-label context and argues that *Sorrell* does not alter the scrutiny by which courts should assess off-label speech regulations. Subpart IV.B addresses the FDA’s argument that it is not regulating speech, but rather is using speech as evidence of the speaker’s “objective intent” and argues that courts should conclude, at least in cases where speech is the primary evidence of one’s intent, that manufacturers’ off-label speech is protected by the First Amendment. Subpart IV.C then argues that the FDA’s speech restrictions fail *Central*

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185. *Id.* at 166–67.

186. *Id.* at 166.

187. *Id.* at 167.

188. *Id.* (“Numerous, less speech-restrictive alternatives are available, as are non-criminal penalties.” (citing *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 372–73 (2002))). The court’s examples of less speech-restrictive alternatives included: directly guiding physicians by disseminating information about which drugs are safe and effective; “develop[ing] . . . warning or disclaimer systems”; creating “safety tiers within the off-label market, to distinguish between” high-risk and low-risk drugs; creating off-label quantity “ceilings or caps on off-label prescriptions”; and regulating off-label prescribing directly. *Id.* at 167–68.

189. *Id.* at 168.

190. *Id.* at 169.

*Hudson* and are unconstitutional. Finally, in light of this conclusion, Subpart IV.D proffers several recommendations as to how Congress and the FDA can bring the current law into conformity with the First Amendment while achieving their objectives of ensuring that prescription medications are safe and effective, readily available, and not overly expensive.

A. *STRICT VS. INTERMEDIATE SCRUTINY: SORRELL'S IMPACT*

Contrary to the conclusion reached by the Second Circuit in *Caronia*, courts should not interpret *Sorrell* to alter the standard of scrutiny applicable to off-label speech regulations, as many aspects of the FDA's off-label restrictions are distinguishable from the Act challenged in *Sorrell*. The *Sorrell* Court was concerned with viewpoint discrimination.<sup>191</sup> *Sorrell* did not purport to overrule *Central Hudson* or alter the level of scrutiny by which courts should adjudge commercial speech cases. *Central Hudson's* less-exacting, intermediate scrutiny serves the important purpose of respecting the political process in matters relating to economic regulation.<sup>192</sup> As noted by Justice Breyer in *Sorrell's* dissent:

The Court . . . applie[s] a . . . lenient approach to ordinary commercial . . . legislation . . . [to] account [for] the need in this area of law to defer significantly to legislative judgment . . . .

. . . [T]o apply a . . . "heightened" . . . review in such cases as a matter of course would risk . . . a retur[n] to the bygone era of *Lochner* . . . .<sup>193</sup>

*Sorrell* should be read narrowly to stand only for the proposition that where laws are objectively viewpoint discriminatory, they are subject to strict scrutiny. However, where the government has identified specific commercial harms, commercial speech regulations should be subject to intermediate scrutiny to afford due respect to the political process. Accordingly, whether *Sorrell* applies in the off-label context turns on whether off-label speech restrictions are objectively viewpoint discriminatory. Given the meaningful differences between the FDA's off-label speech restrictions and the Act challenged in *Sorrell*, it is clear that the FDA's restrictions are not viewpoint discriminatory.

As in *Sorrell*, the FDA's regulations restrict speech content by affecting marketing and imposing burdens on specific speakers by applying exclusively to drug manufacturers. However, unlike *Sorrell*, agency findings do not indicate that the FDA's off-label restrictions are intended to "advance

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191. *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2663 (2011); see also *supra* Part II.B.2.b.

192. See *Sorrell*, 131 S. Ct. at 2678 (Breyer, J., dissenting).

193. *Id.* at 2674–75 (quoting *Cent. Hudson Gas & Elec. Corp v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557, 589 (1980) (Rehnquist, J., dissenting)).

[one] side of a debate.”<sup>194</sup> Unlike *Sorrell*, the FDA’s regulations do not prohibit inherently factual speech or the dissemination of objectively verifiable prescribing information. Rather, the FDA’s regulations make sure that drug manufacturers’ claims are substantiated.<sup>195</sup> As the government argued in its brief in *Caronia*, the FDA’s regulations “provide the public with reliable information about the medicines they are using, in much the same fashion that securities laws provide the public with reliable information about the investments that they are making.”<sup>196</sup> They ensure that the message is factual. Absent the FDA, there is no filter checking for truthfulness, and the truth may essentially be purchased by pharmaceutical companies who often finance the studies upon which they subsequently rely to substantiate their claims. The FDA’s restrictions are designed to get off-label uses on-label to ensure that much-needed safety and efficacy information is generated in the first place and to act as a check to ensure that the studies conducted by drug manufacturers are reliable and factually accurate.<sup>197</sup>

Moreover, unlike *Sorrell*, the FDA’s regulations are neither ineffective nor perplexingly underinclusive. They are at least partly effective, as they provide a substantial incentive for drug manufacturers to conduct off-label clinical trials.<sup>198</sup> Moreover, they are not underinclusive because “drug manufacturers . . . form the entirety of those speakers that could . . . undermine the new drug approval process.”<sup>199</sup> Given these distinguishing factors, courts should not follow *Caronia*’s lead in requiring some form of heightened standard of review beyond that of *Central Hudson*, but should continue to subject off-label speech regulations to *Central Hudson*’s intermediate scrutiny.

#### B. EVIDENCE OF INTENT VS. PROTECTED SPEECH

Post-*Sorrell*, as a preliminary matter, a court must determine whether the FDA’s off-label regulations restrict speech, or whether the FDA merely uses speech as evidence of drug manufacturers’ intent that their drugs be used off-label.<sup>200</sup> The FDA contends it has not restricted speech, but rather uses

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194. *See id.* at 2672 (majority opinion).

195. *See* United States v. Caronia, 703 F.3d 149, 181 (2d Cir. 2012) (Livingston, J., dissenting).

196. Supplemental Brief for the United States at 9, United States v. Caronia, 703 F.3d 149 (2d Cir. 2012) (No. 09-5006-cr), available at <http://www.hpm.com/pdf/blog/US%20Caronia%20Supp%20Brief.pdf>.

197. *See id.* at 10.

198. *Caronia*, 703 F.3d at 178 (Livingston, J., dissenting); Wash. Legal Found. v. Friedman (*WLF I*), 13 F. Supp. 2d 51, 70 (D.D.C. 1998).

199. *Caronia*, 703 F.3d at 179 (Livingston, J., dissenting).

200. *See id.* at 160–61 (majority opinion); United States v. Caputo, 288 F. Supp. 2d 912, 919 (N.D. Ill. 2003); *WLF I*, 13 F. Supp. 2d at 59, 62.

speech as evidence of intent. However, as Klasmeier and Redish note, this is a hollow assertion:

[T]here is no indication that the FDA has *ever* pursued a manufacturer for selling its drug with knowledge that it will be used for off-label purposes, absent off-label promotion. Where a manufacturer does not seek to advertise, the FDA makes no objection, *though there can be no doubt that the manufacturer is aware when it sells its product that it will be used off-label*. . . . [Thus,] the FDA is not seeking to regulate the *act* of sale for the purpose of off-label use; it is, rather, . . . seeking to regulate solely the expression itself—nothing more, nothing less.<sup>201</sup>

The *Caronia* court was correct in concluding that the FDA does not outright ban speech, but it was also correct in noting that the government was prosecuting the defendant solely for his speech, and that, therefore, the First Amendment applied. However, the *Caronia* court left open the question of whether additional non-speech evidence indicating *Caronia*'s intent would have altered this calculus.<sup>202</sup> Given that in most cases intent is proven by drug manufacturers' speech, that off-label restrictions do outright ban some forms of speech,<sup>203</sup> and the severe criminal consequences that accompany a violation of off-label restrictions,<sup>204</sup> courts should follow *Caronia*'s lead and conclude that these speech restrictions implicate the First Amendment, especially where the only evidence of intent is speech.

### C. CENTRAL HUDSON APPLIED

As the *WLF I* court, the *Caputo* court, and the *Caronia* court recognized, the government's off-label speech restrictions easily satisfy *Central Hudson*'s initial requirement, that the speech be both lawful and not misleading.<sup>205</sup> The speech is lawful because off-label use is lawful, meaning the speech promotes lawful activity.<sup>206</sup> Whether drug manufacturers' unsubstantiated assertions are inherently misleading poses a closer question. However, as other parties, including the FDA, often disseminate the same information, it

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201. Klasmeier & Redish, *supra* note 27, at 343.

202. See *Caronia*, 703 F.3d at 161.

203. See *supra* notes 42–43 and accompanying text.

204. Kristie LaSalle, Note, *A Prescription for Change: Citizens United's Implications for Regulation of Off-Label Promotion of Prescription Pharmaceuticals*, 19 J.L. & POL'Y 867, 893 (2011) (arguing that off-label restrictions function as a prior restraint, given the harsh criminal sanctions imposed).

205. *Caronia*, 703 F.3d at 165; *Caputo*, 288 F. Supp. 2d at 920–21; *WLF I*, 13 F. Supp. 2d at 65–69.

206. See, e.g., *Caronia*, 730 F.3d at 165 (“[P]romoting off-label drug use concerns lawful activity (off-label drug use), and the promotion of off-label drug use is not in and of itself false or misleading.”).

is unlikely that the speech is inherently misleading.<sup>207</sup> Moreover, given that physicians are a “sophisticated audience” and a gateway between patients and prescription drugs, drug manufacturer marketing efforts are likely not inherently misleading.<sup>208</sup>

In applying *Central Hudson*’s first prong, courts should find the government has a “substantial interest” in “[p]reserving the effectiveness and integrity of the FDCA’s new drug approval process . . . and . . . has every reason to want as many drugs as possible to be subject to that approval process.”<sup>209</sup> The *Caronia* majority conceptualized the FDA’s interest in getting off-label uses on-label to be substantial only insofar as the government’s efforts successfully reduced patient exposure to potentially harmful drugs.<sup>210</sup> However, this view of the FDA’s interest overlooks the stark reality that it is practically impossible to know which drugs may prove unsafe or ineffective until they have been adequately tested. The FDA’s interest is in ensuring that consumers may rely on substantiated information.<sup>211</sup> Thus, the FDA has an interest in incentivizing drug manufacturers to get off-label uses on-label or to conduct additional clinical trials. Unlike *Thompson* and *Sorrell*, the government is typically not trying to prevent individuals from making decisions based on factual information; the government is trying to ensure that the information is factual. FDA regulations are not based on a “fear that people would make bad decisions if given truthful information.”<sup>212</sup>

Addressing the second *Central Hudson* prong, courts should conclude that the FDA’s substantial interest, properly understood, is directly advanced through regulation of off-label speech. The *Sorrell* Court suggested that Vermont’s law did not directly advance the FDA’s interest because Vermont sought to achieve its goals “by diminishing detailers’ ability to influence prescription decisions.”<sup>213</sup> Some may argue the FDA’s restrictions seek to achieve its goals in a similarly “indirect” fashion because the regulations incentivize drug manufacturers to get off-label uses on-label by restricting manufacturers’ ability to persuade physicians to prescribe off-label rather than regulating physician’s off-label prescribing practices directly. However, the FDA’s restrictions are more direct than in *Sorrell*, because the FDA regulates drug manufacturer speech, whereas the Act in *Sorrell* was one step

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207. *WLF I*, 13 F. Supp. 2d at 66–68.

208. *Id.* at 63; *see also Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2671 (2011) (“Th[at] precept[] appl[ies] with full force when the audience, in this case prescribing physicians, consists of ‘sophisticated and experienced’ consumers.” (quoting *Edenfield v. Fane*, 507 U.S. 761, 775 (1993))).

209. *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 369 (2002).

210. *Caronia*, 703 F.3d at 166.

211. *Id.* at 177–78 (Livingston, J., dissenting).

212. *Thompson*, 535 U.S. at 374.

213. *Sorrell*, 131 S. Ct. at 2670.

further removed in that it merely made manufacturer marketing efforts less effective through limiting the information that drug manufacturers could use to craft their messages.<sup>214</sup> Given this distinction and the way the FDA's regulations do in fact advance its interest, courts should conclude that the FDA's interests are directly advanced by its regulation of off-label speech.

*Central Hudson's* final prong has, in the past, posed the greatest challenge for the FDA in defending its off-label speech restrictions.<sup>215</sup> First, the FDA's restrictions are overinclusive, in that they affect considerable amounts of speech beyond what is necessary to advance the FDA's interest in incentivizing drug manufacturers to get off-label uses on-label.<sup>216</sup> For example, FDA regulations burden manufacturer efforts to disseminate off-label safety information to physicians who are already prescribing off-label.<sup>217</sup> Such speech likely does not increase manufacturer sales; therefore, prohibiting it does not affect drug manufacturers' incentives to get off-label uses on-label.<sup>218</sup> Further, FDA regulations have a chilling effect on some on-label speech, as the intended-use provisions criminalize any objective intent that a drug be distributed in commerce for an off-label purpose.<sup>219</sup> Problematically, this objective intent can be shown by on-label speech made in off-label contexts.<sup>220</sup> Finally, as noted above, off-label regulations especially affect speech where a drug is widely prescribed off-label and where off-label prescribing is relatively infrequent. In both cases, drug manufacturers are unlikely to expend the resources to get off-label uses on-label merely to gain the ability to advertise, as it is difficult to forecast whether advertising will generate sufficient sales to cover the cost of

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214. See *id.* at 2671 (asserting that restricting advertising is more direct than reducing the effectiveness of advertising by limiting access to information).

215. See *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51, 59, 62 (D.D.C. 1998).

216. See Memorandum of Law in Support of Motion for Preliminary Injunction at 26, *Allergan, Inc. v. United States*, No. 1:09-cv-01879 (D.D.C. dismissed Oct. 14, 2010), available at <http://druganddevicelaw.net/Allergan%20Off-label%20PI%20Motion.pdf>.

217. See *id.* at 25–26.

218. For example, Allergan produces the drug Botox, which is commonly used to counteract facial wrinkling and is also frequently prescribed off-label to counteract muscle spasms. *Id.* at 13. There is evidence that this off-label use poses health risks, and Allergan sought to inform physicians about the safety issues related to the practice. *Id.* at 13–15. However, Allergan was unable to do so because of FDA regulations. *Id.*

219. See 21 C.F.R. §§ 201.100(c)(1), 201.128 (2013).

220. See *supra* notes 68–71 and accompanying text. Because Megace is widely prescribed off-label, Par cannot promote Megace's on-label uses because that amounts to a manifestation of its intent that its drug be prescribed off-label because the FDA could use Par's on-label speech and knowledge of widespread off-label prescribing practices as evidence of its intent that Megace be prescribed off-label. Par-Pharm Plaintiff's Memorandum, *supra* note 3, at 11. Par wishes to speak to oncologists (with off-label patients) who also encounter AIDS patients (on-label) about the benefits of Megace as it relates to AIDS patients; however, the FDA's regulations effectively preclude Par from doing this. *Id.*

subsequent clinical trials. Thus, in many instances, the FDA's incentive simply does not work.<sup>221</sup>

Second, *Thompson* is clear that the government bears the burden of explaining why non-speech-restrictive alternatives would not suffice.<sup>222</sup> Unlike the *Caputo* court, which placed the burden on the defendant to explain how alternative options would achieve the FDA's desired goal, the *Caronia* court was correct in considering less restrictive regulations and requiring the FDA to explain why some combination of alternatives was insufficient.<sup>223</sup> Many commentators have suggested less speech-restrictive alternatives, such as "time, place, and manner" restrictions,<sup>224</sup> full disclosure,<sup>225</sup> tax incentives,<sup>226</sup> additional patent protection for on-label uses,<sup>227</sup> and "preempt[ing] product liability cases for products that receive FDA approval."<sup>228</sup> Accordingly, given the overinclusiveness of the FDA's speech ban, the availability of alternative options, and the fact that the FDA bears the burden to explain why less-restrictive options are inadequate, courts should find the FDA's speech restrictions fail *Central Hudson's* final prong and, therefore, the FDA's restrictions are unconstitutional.

#### D. SOLUTIONS

Congress and the FDA must take action to create less speech-restrictive incentives to get off-label uses on-label, because compelling additional

221. "The relatively small number of supplements that are submitted for additional uses, compared to the very large number of off-label uses that occur, suggest that the incentive isn't particularly successful . . . . Given the volume of information about off-label uses that is available to speakers other than manufacturers, it is not surprising that the incentive is relatively weak." Kate Rawson, *Off-Label Changes Coming? Sorrell Ruling Prompts New Legal Challenges*, RPMREPORT, Oct. 2011, at 1, 6 (quoting Richard Cooper, former FDA chief counsel) (internal quotation marks omitted), available at <http://www.cohealthcom.org/2011/10/24/rpm-report-pandora%E2%80%99s-box-officially-open-as-new-legal-challenges-to-fda%E2%80%99s-off-label-restrictions-begin> (follow "Off Label Changes Coming" hyperlink).

222. *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 373 (2002) ("[I]t is well established that 'the party seeking to uphold a restriction on commercial speech carries the burden of justifying it.'" (quoting *Edenfield v. Fane*, 507 U.S. 761, 770 (1993))).

223. See *id.* ("The Government has not offered any reason why these possibilities, alone or in combination, would be insufficient . . . ." (emphasis added)).

224. Bennett, *supra* note 14, at 488.

225. *Wash. Legal Found. v. Friedman (WLF I)*, 13 F. Supp. 2d 51, 73 (D.D.C. 1998); see also LaSalle, *supra* note 204, at 909.

226. *United States v. Caronia*, 576 F. Supp. 2d 385, 401 n.12 (E.D.N.Y. 2008), *vacated*, 703 F.3d 149 (2d Cir. 2012).

227. *Id.*

228. Frederick R. Ball et al., *The First Amendment and Off-Label Promotion: Why the Court in United States v. Caronia Got It Wrong*, BENDER'S HEALTH CARE LAW MONTHLY, Apr. 2009, at 1, 12, available at [http://www.duanemorris.com/articles/static/ballduffyrussakoff\\_bendero409.pdf](http://www.duanemorris.com/articles/static/ballduffyrussakoff_bendero409.pdf); see also Ralph F. Hall & Elizabeth S. Sobotka, *Inconsistent Government Policies: Why FDA Off-Label Regulation Cannot Survive First Amendment Review Under Greater New Orleans*, 62 FOOD & DRUG L.J. 1, 46 (2007).

clinical trial data is essential to ensure that physicians and patients are able to make fully informed, well-educated decisions. In considering less-restrictive alternatives, Congress must consider the sub-objectives encompassed by the FDA's larger goal of promoting the public health and welfare. First, the FDA aspires to ensure that drugs are safe and effective for each of their intended uses.<sup>229</sup> Second, the FDA seeks to ensure that new and innovative drugs are timely made available for consumer use.<sup>230</sup> Third, the FDA aims to ensure that clinical trial data and scientific information are readily available, allowing doctors and patients to make well-informed decisions.<sup>231</sup> Finally, the FDA seeks to achieve these objectives without substantially increasing drug prices for consumers. Attentive to these objectives, the remainder of this Note suggests how Congress and the FDA may create incentives to get off-label uses on-label in conformance with the First Amendment.

### 1. Less Restrictive Speech Regulation

As noted, one major problem with the FDA's restrictions under *Central Hudson's* third prong is that they are overinclusive.<sup>232</sup> To address this problem, the FDA could create safe harbors rendering drug manufacturers immune from prosecution in circumstances where restricting their off-label speech does not further the FDA's interests.<sup>233</sup> This would likely not bring the FDA's regulations into total conformity with the First Amendment, as non-speech alternatives may still prove effective. However, creating safe harbors would be a step in the right direction and better balance the totality of the FDA's interests.

For example, as noted above, one way in which the FDA's regulations are overinclusive is that they restrict manufacturers' efforts to disseminate off-label safety information to physicians who are already prescribing off-label.<sup>234</sup> Considering the FDA's objectives, restricting this speech creates little incentive for drug manufacturers to conduct subsequent clinical trials. This is so because, as the dissemination of such speech does not likely increase off-label prescribing rates nor manufacturer profits, the FDA's

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229. See 21 U.S.C. § 393(b)(2)(B) (2012).

230. See *id.* § 393(b)(1).

231. Cf. David M. Fritch, Note, *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 J. MED. & L. 315, 318 (2005) (discussing the importance of information in the context of the FDA's role).

232. See *supra* notes 216–18 and accompanying text.

233. See Jose Sierra, *A First Amendment Safe Harbor for Off-Label Promotion—The Right Course for the Government*, PHARMARISC.COM (Dec. 21, 2012), <http://pharmarisc.com/2012/12/a-first-amendment-safe-harbor-for-off-label-promotion-the-right-course-for-the-government> (arguing that the FDA should enact safe harbors to protect drug manufacturers' First Amendment rights).

234. See *supra* notes 215–21 and accompanying text.

restrictions serve only to stifle the dissemination of important safety information. This is not in the public's best interests. Accordingly, the FDA should create a safe harbor for drug manufacturers that distribute off-label safety information to physicians who are either already prescribing their products off-label, or who could reasonably be expected to be prescribing their products off-label, as substantiated by specific, verifiable criteria. This would give drug manufacturers leeway to disseminate off-label safety and best-practice information in cases in which speech is unlikely to lead to increased profits sufficient to cover the costs of subsequent clinical trials.

Alternatively, as the FDA's speech restrictions stem from its fear that drug manufacturers' off-label claims will be unsubstantiated, the FDA could create a safe harbor that protects drug manufacturers' "truthful and non-misleading off-label speech," evidenced by external corroborating indicia.<sup>235</sup> Drug manufacturers could demonstrate that their speech is sufficiently "truthful and non-misleading" through showing that "the off-label use is medically accepted (as evidenced by inclusion in recognized medical compendia) [or] reimbursed by Medicare, Medicaid [or] other federal healthcare programs," as reimbursement by these sources indicates that manufacturer claims are not merely anecdotal assertions.<sup>236</sup> These safe harbors address the over-inclusiveness of the FDA's regulations and better serve the public interest.

## 2. Economic Incentives

In addition to creating safe harbors, or in place of off-label speech restrictions, the FDA could create economic incentives to get off-label uses on-label.<sup>237</sup> This incentive system would be the best way to avoid First Amendment concerns. Congress or the FDA could: (1) create incentives for doctors to prescribe on-label via Medicare and Medicaid; (2) create economic incentives for drug manufacturers to get off-label uses on-label, either through the tax code or the patent laws; and/or (3) tax drug manufacturers in proportion to the incidence of physicians' off-label prescribing of their drugs in order to fund FDA's own off-label research efforts.

First, Congress could increase incentives for doctors to prescribe on-label via Medicare and Medicaid. Under current law, Medicare and Medicaid reimburse patients when their doctors prescribe drugs off-label.<sup>238</sup> The government could simply stop doing this, either entirely or selectively, and "require that any healthcare provider submitting a claim for Medicare or Medicaid reimbursement must disclose the use of any off-label

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235. See Sierra, *supra* note 233.

236. *Id.*

237. Hall & Sobotka, *supra* note 228, at 45-46.

238. *Id.* at 45.

product.”<sup>239</sup> This would reduce physicians’ willingness to prescribe off-label and pressure drug manufacturers to get off-label uses on-label.<sup>240</sup> However, this solution is problematic because it either deters doctors from ever prescribing off-label, which can be beneficial for patients, or it requires an agency to select the specific off-label uses government insurance will cover.<sup>241</sup> As one commentator notes, this option “would likely . . . cause public outcry,” and Congress is unlikely to adopt it for that reason.<sup>242</sup>

Second, a more viable option may be for Congress to create economic incentives, either through the tax code or the patent system.<sup>243</sup> Creating a tax credit or rebate for drug manufacturers to reduce subsequent clinical trial costs would give manufacturers an incentive to get off-label uses on-label without restricting speech. Moreover, this method would give Congress flexibility, as the credit could be adjusted to create the proper incentive. As an alternative, granting additional patent protection for on-label uses could also provide manufacturers with an incentive to get off-label uses on-label. This solution would provide a proper incentive because, even where doctors are widely prescribing off-label, on-label profits would prove more lucrative. However, it may have the adverse effect of increasing drug prices for consumers. This solution would also give Congress flexibility, as the scope of additional protection could be adjusted in pursuit of the ideal incentive structure.

Finally, “[n]othing in the First Amendment precludes [the] FDA from requiring manufacturers to obtain information concerning the prevalence of off-label use of their products.”<sup>244</sup> Congress could require pharmacies to report any incidence of off-label prescribing to the FDA and drug manufacturers, and then tax drug manufacturers in proportion to that use. These taxes could fund the FDA’s own clinical trial efforts. If clinical trials proved the off-label uses to be unsafe or ineffective, drug manufacturers would no longer be taxed for doctors’ continued off-label prescribing practices, as the aim is not to punish drug manufacturers, but to generate safety and efficacy information. This solution would have the adverse effect of increasing the price of drugs for consumers and may also prove impracticable, as it would require the compilation of large amounts of data. However, if feasible, this option would allow drug manufacturers to disseminate important safety information, and either provide the FDA with the means to engage in efficacy testing or encourage manufacturers to conduct subsequent trials on their own.

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239. *Id.*

240. *See id.* at 46.

241. *Id.*

242. *Id.*

243. *See* Ball et al., *supra* note 228, at 12.

244. Blackwell & Beck, *supra* note 2, at 459.

In summary, Congress or the FDA could: (1) increase incentives for doctors to prescribe on-label via Medicare or Medicaid; (2) create economic incentives for drug manufacturers to get off-label uses on-label, either through the tax code or patent law; or (3) tax drug manufacturers in proportion to the incidence of physicians' off-label prescribing, in order to fund the FDA's own off-label research efforts. The first option may prove difficult, as it would intrude on the doctor-patient relationship, and the third option may prove impracticable. Therefore, the second option, using the tax code and patent system to create economic incentives, is a preferable approach because it gives Congress and the FDA the flexibility to strike an optimum incentive structure and the leeway to balance competing interests.

### 3. Drawing the Line Elsewhere

Finally, Congress could also incentivize drug manufacturers to get off-label uses on-label without violating the First Amendment by referencing the conduct of third parties. As several commentators suggest, Congress could "require companies to seek FDA approval for products that the manufacturer knows [or should know] are being used in a significant off-label manner."<sup>245</sup> For example, the "FDA could require manufacturers to seek FDA approval of off-label uses if such uses reach specified statistical thresholds—either by pure volume of off-label prescriptions or by off-label use as a percentage of total product sales."<sup>246</sup> The FDA could also require drug manufacturers to seek FDA approval of off-label uses when a certain number of products liability suits have been filed, as this would evidence that further clinical trials relating to particular off-label uses are necessary. Although this solution would not be effective alone because, in some cases, the filing of products liability suits indicates the damage has already been done, requiring subsequent testing combined with other economic incentives may prove effective.

## V. CONCLUSION

The war on the FDA's off-label speech restrictions is only beginning. While the implications of the Supreme Court's recent decision in *Sorrell v. IMS Health Inc.* remain unclear, courts should not interpret *Sorrell* as requiring courts to apply strict scrutiny to the FDA's off-label regulations. Courts would be ill-advised to interpret *Sorrell* so broadly. *Central Hudson's* intermediate scrutiny, commercial speech framework protects First Amendment rights in the commercial realm while paying due respect to the political process. Nevertheless, the FDA's off-label speech restrictions likely

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<sup>245</sup> Ball et al., *supra* note 228, at 12; *see also* Blackwell & Beck, *supra* note 2, at 459–60 (discussing the FDA's authority to regulate that drug companies collect information on off-label use).

<sup>246</sup> Blackwell & Beck, *supra* note 2, at 459.

do not pass *Central Hudson*'s final prong. Therefore, Congress and the FDA must create adequate incentives to get off-label uses on-label and to bring current law into conformity with the First Amendment. Congress and the FDA could achieve their objectives in one of several constitutionally permissible ways: by restricting less speech, creating economic incentives, drawing the line elsewhere, or a combination of these options. These less speech-restrictive alternatives could bring the FDA's regulations into conformity with the First Amendment and better serve the public health and welfare.