



# Promotion of Unapproved Uses of Approved Drugs and Devices: An Analysis under the First Amendment

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# Introduction

Government has played an important role in assuring the integrity of the food supply for centuries.<sup>1</sup> Although originally an effort to control fraud in the marketplace, regulation evolved to protect against unsafe food,<sup>2</sup> and eventually to assure the nutritional integrity of food.<sup>3</sup> Because the first drugs were food products, regulating food and drugs together made sense. In the United States, the first comprehensive federal legislation regulating food and drugs, the Pure Food and Drug Act of 1906,<sup>4</sup> focused on the purity and quality of products and the accuracy of their branding.<sup>5</sup> While the 1906 Act did contribute to the safeguarding of the public's health, the Act had several limitations,<sup>6</sup> and eventually demand for a new regulatory system mounted.<sup>7</sup> Congress strengthened legal control over the efficacy and safety of drugs with the passage of the Food, Drug, and Cosmetic Act of 1938 (FD&C Act).<sup>8</sup> Under the FD&C Act, FDA has broad authority to regulate and has enjoyed immense regulatory power.<sup>9</sup> Most of the Act's operative provisions describe circumstances under which a food, drug, or cosmetic would be subject to FDA enforcement action because of adulteration or misbranding.<sup>10</sup>

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<sup>1</sup>See Peter Barton Hutt, *Government Regulation of the Integrity of the Food Supply*, 4 *Annual Review of Nutrition* 1 (1984), in *FOOD & DRUG LAW: CASES & MATERIALS* (Peter B. Hutt & Richard A. Merrill, eds., 1991), at 1.

<sup>2</sup>See *id.*

<sup>3</sup>See *id.*

<sup>4</sup>Pure Food and Drug Act of 1906, ch. 3915, 34 Stat. 768 (repealed 1938).

<sup>5</sup>See Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 *FLORIDA LAW REVIEW* 181, 183, citing ch. 3915, §§ 1-12, 34 Stat. at 768-72. See also *FOOD & DRUG LAW*, *supra* note 1, at 4, 9.

<sup>6</sup>See 1917 Report of the USDA Bureau of Chemistry, in *FOOD & DRUG LAW*, *supra* note 1, at 10-11. Limitations included the lack of (1) legal standards for food, (2) authority to inspect warehouses, and (3) any restriction on the use of poisons in drugs. See *id.*

<sup>7</sup>See *id.* at 11.

<sup>8</sup>See Salbu, *Off-Label Use*, *supra* note 5, at 183, citing Pub. L. No. 52-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-392 (1997)).

<sup>9</sup>See Anne Marie Murphy, "It's Time to Make a Good Agency Better": The Food and Drug Administration Modernization Act of 1997 and the First Amendment, 53 *FOOD & DRUG L.J.* 603, 616.

<sup>10</sup>See *FOOD & DRUG LAW*, *supra* note 1, at 12.

The FD&C Act has been amended over one hundred times since 1938,<sup>11</sup> at times expanding and other times constricting FDA authority. For example, the rigor of external control was expanded with the passage of the Drug Amendments of 1962<sup>12</sup> and the Medical Device Amendments in 1976.<sup>13</sup> One author notes that, over a period of less than sixty years, the pharmaceuticals market was transformed to a closely regulated environment.<sup>14</sup> Nevertheless, FDA has also been subject to enactments curtailing its power, most notably in the 1980s and 1990s. This movement away from the trend of escalating administrative authority matched the deregulatory atmosphere of the Reagan administration and was a response to activists' demands for expedited marketing of new HIV and AIDS treatments.<sup>15</sup> Early AIDS-era reforms included the development of the use of investigational new drugs for treatment, fast-track approvals, and parallel-track investigational drugs.<sup>16</sup> In addition, Congress further deregulated the already loosely governed market for dietary supplements by passing the Dietary Supplement Health and Education Act of 1994 (DSHEA).<sup>17</sup> More recently, regulatory and legislative changes have focused on the area of pharmaceutical marketing. FDA has initiated changes that have broadened the ways in which drug manufacturers advertise pharmaceutical products directly to consumers.<sup>18</sup> Consequently, many of the components of this era of change have increased consumer access to drugs and related products, and expanded freedom in the manufacture and marketing of those products.<sup>19</sup>

In 1997, Congress passed the Food and Drug Administration Modernization Act (FDAMA), amending the

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<sup>11</sup>See *Summary of FDAMA*, Covington & Burling, at 5.

<sup>12</sup>See Salbu, *Off-Label Use*, supra note 5, at 183, citing Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified as amended in scattered sections of 21 U.S.C. §§ 301-381 (1997)). The Drug Amendments transformed a system of premarket notification into one that requires individual premarket approval of the safety and effectiveness of every new drug, thereby fundamentally restructuring the way in which FDA regulated new medicines. See *FOOD & DRUG LAW*, supra note 1, at 13.

<sup>13</sup>See *FOOD & DRUG LAW*, supra note 1, at 13. The Amendments transformed FDA's approach to regulation of medical devices and substantially enlarged the array of regulatory tools available to the Agency. See *id.*

<sup>14</sup>See Salbu, *Off-Label Use*, supra note 5, at 183.

<sup>15</sup>See *id.* at 193, citing Michael C. Dorf and Charles F. Sabel, *A Constitution of Democratic Experimentalism*, 98 Colum. L. Rev. 267, 361 (1998) (associating the Reagan administration with an era of deregulation) and Phillip J. Hiltz, *How the AIDS Crisis Made Drug Regulators Speed Up*, New York Times, Sept. 24, 1989, at E5 (noting the connection between AIDS activism and FDA reforms).

<sup>16</sup>See Salbu, *Off-Label Use*, supra note 5, at 184.

<sup>17</sup>See *id.*

<sup>18</sup>See *id.* (citations omitted).

<sup>19</sup>See *id.* at 183, citing Steven R. Salbu, *The FDA and Public Access to New Drugs: Appropriate Levels of Scrutiny in the Wake of HIV, AIDS, and the Diet Drug Debacle*, 79 B.U. L. REV. 93 (1999).

FD&C Act and the biological products provisions in section 351 of the Public Health and Service Act.<sup>20</sup> Viewed as a whole, the FDAMA represents a substantial change in the existing law.<sup>21</sup> While the law is comprehensive, some provisions specifically relate to manufacturers' ability to promote off-label uses of approved products. In 1999, three cases signaled a major change in the way FDA can regulate, affirming the theme of increased consumer access to information and increased freedom in the marketing of products and services regulated by FDA. In these cases, courts found various FDA Guidance Documents,<sup>22</sup> sections of FDAMA, and FDA's implementation of the law to be in contravention of the First Amendment freedom of speech. Relying on the commercial speech doctrine, courts held in favor of a more liberalized approach to the dissemination of information with respect to off-label use, services for compounded drugs, and health claims for dietary supplements. This paper seeks (1) to provide the background necessary to understand current commercial speech jurisprudence; (2) to explore the First Amendment analysis in recent cases against FDA; (3) to examine the landscape of food and drug law and FDA's regulation with respect to the promotion of prescription drugs and medical devices; and (4) to discuss the viability of other FDA policies on off-label promotion. In light of the recent decisions and the expansion of ways to provide information to consumers, the paper argues in favor of increased consumer access to information and the expansion of manufacturers' ability to provide information, within certain parameters.

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<sup>20</sup>See *Summary of FDAMA*, *supra* note 11, at 1.

<sup>21</sup>See *id.* at 9.

<sup>22</sup>§ 701(h)(1)(A) of FDAMA requires FDA to develop guidance documents with public participation and ensure that such written documents are publicly available. Although the guidance documents do not create or confer any rights for or on any person, they do represent the views of FDA on matters under its jurisdiction. See *Summary of FDAMA*, *supra* note 11, at 91-92.

## I. First Amendment Background

### A.

#### Commercial Speech Doctrine

The Supreme Court has never held that all forms of communication are constitutionally protected.<sup>23</sup> Traditionally, most kinds of “commercial speech” were viewed as being an unprotected category, outside the scope of the First Amendment.<sup>24</sup> It was not until 1976 that the Court formally abandoned the traditional rule and held that even “purely commercial” speech is entitled to First Amendment protection.<sup>25</sup> In *Virginia State Board of Pharmacy v. Virginia Consumer Council*, the Court struck down Virginia’s ban on advertising prescription drug prices as a violation of the First Amendment.<sup>26</sup> Importantly, the Court concluded that the First Amendment forbids the State from deciding that ignorance is preferable to the free flow of information.<sup>27</sup> The Court rejected Virginia’s contention that drug price advertising could trigger distorted perceptions and misguided conduct, noting that the First Amendment did not countenance “this highly paternalistic approach.”<sup>28</sup> Nevertheless, the Court indicated that, although commercial speech is entitled to protection, the protection might be less extensive than for other

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<sup>23</sup>The First Amendment does not cover certain utterances, such as obscenity, defamation, and “fighting words.” See *Beauharnais v. Illinois*, 343 U.S. 250, 266 (1952) (obscenity); *Chaplinsky v. New Hampshire*, 315 U.S. 568, 572 (1942) (defamation); *Roth v. U.S.*, 354 U.S. 476, 485 (1957) (“fighting words”).

<sup>24</sup>See *Valentine v. Chrestensen*, 316 U.S. 52 (1942). The traditional view was that “purely commercial advertising” was not entitled to any First Amendment protection, and could therefore be subjected to governmental regulation in the same way as any other type of business activity. See *id.*

<sup>25</sup>See *Virginia State Board of Pharmacy v. Virginia Consumer Council*, 425 U.S. 748 (1976) (hereinafter “*Virginia Pharmacy*”). See Murphy, “It’s Time to Make a Good Agency Better,” *supra* note 9, at 616 or 619?. See also Edmund Polubinski III, *Closing the Channels of Communication: A First Amendment Analysis of the FDA’s Policy on Manufacturer Promotion of “Off-Label” Use*, 83 VA. L. REV. 181, footnote 114.

<sup>26</sup>See *Virginia Pharmacy*, 425 U.S. 748 (year). See also Nat Stern, *In Defense of the Imprecise Definition of Commercial Speech*, 58 MD. L. REV. 55, 59 (1999).

<sup>27</sup>See *id.*

<sup>28</sup>*Id.* at 769-770. See also Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 60-61.

types of speech.<sup>29</sup> The Court noted two attributes of commercial speech justifying greater regulation that would be acceptable for other forms of expression. First, the relative objectivity of commercial speech supports an expectation that commercial speakers can verify the truth of their message.<sup>30</sup> Second, the “hardiness” of commercial speech, based on the dependence of profits on advertising, decreases the worry that commercial speech will be hampered by regulation promoting truthful commercial information.<sup>31</sup>

The anti-paternalistic theme emerged again as a major factor in *Bates v. State Bar of Arizona*, where the Court ruled that a state bar could not prohibit an attorney’s advertising the price of routine legal services.<sup>32</sup> The State argued that advertising of legal services is inevitably misleading because of the incomplete information provided by the advertising.<sup>33</sup> The Supreme Court again expressed its skepticism of justifications for suppressing truthful information “based on the benefits of public ignorance.”<sup>34</sup> Although in the next term, the Court sustained a state’s bar on the ability of attorneys to solicit clients in person,<sup>35</sup> the Court did not repudiate the “anti-paternalistic heart of Virginia Pharmacy.”<sup>36</sup> In trying to define the limits of the protection for commercial speech, the Court attempted to articulate a “common sense” distinction between permissible and non-permissible restrictions on commercial speech.<sup>37</sup> One author argues that the Court was not trying to create a non-regulable category of speech, but rather was attempting to illustrate the more limited nature of protection offered to commercial speech.<sup>38</sup> The Supreme Court’s current approach recognizes an intermediate category meriting its own analysis.<sup>39</sup>

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<sup>29</sup>Note that false or misleading advertising could be prohibited. Similarly, broader regulation of “time, place, and manner” might be justified, and the strong presumption against prior restraints might not apply.

<sup>30</sup>See Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 61, discussing *Virginia Pharmacy*, 425 U.S. at 772.

<sup>31</sup>See *Id.*, discussing *Virginia Pharmacy*, 425 U.S. at 772.

<sup>32</sup>See 433 U.S. 350 (1977).

<sup>33</sup>See Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 62, discussing *Bates*, 433 U.S. at 375. Because potential clients will not know which specific services they need, their decision-making capacity is diminished. See *id.*

<sup>34</sup>*Bates*, 433 U.S. at 375.

<sup>35</sup>See *Ohralik v. Ohio State Bar Assn.*, 436 U.S. 447 (1978).

<sup>36</sup>Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 63.

<sup>37</sup>Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1014, citing *Ohralik*, 436 U.S. at 455-56, quoting *Virginia Pharmacy*, 425 U.S. at 761.

<sup>38</sup>See *id.* at 1015.

<sup>39</sup>See *id.* at 1010.

In 1980, the Court promulgated a formal four-part test to determine whether a given regulation of commercial speech violates the First Amendment:

At the outset, we must determine whether the expression is protected by the First Amendment. For commercial speech to come within that provision, it at least must concern lawful activity and not be misleading. Next, we ask whether the asserted government interest is substantial. If both inquiries yield positive answers, we must determine whether the regulation directly advances the government interest asserted, and whether it is not more extensive than is necessary to serve that interest.<sup>40</sup>

Applying the four-part test, the Court struck down a state’s blanket ban on advertising by an electric utility to promote the use of electricity.<sup>41</sup> Under the *Central Hudson* standard, the first question asks whether the targeted speech is constitutionally protected.<sup>42</sup> The Court held in *Central Hudson* that commercial speech receives protection only to the extent that it concerns lawful activity and is not misleading,<sup>43</sup> where misleading speech is “communication more likely to deceive the public than to inform it.”<sup>44</sup> In more recent cases, the Court has clarified that this portion of the test covers only “inherently misleading” speech,<sup>45</sup> subjecting speech that is only “potentially misleading” to the balancing inquiry of the remainder of the *Central Hudson* test.<sup>46</sup> To evaluate whether speech is “inherently misleading,” courts will consider whether the speech is more likely to deceive the public than inform it,<sup>47</sup> whether there are substantial “possibilities for deception,”<sup>48</sup> and whether experience has shown that such advertising is subject to abuse.<sup>49</sup>

The second inquiry evaluates the government’s interest in restricting the speech: is the restriction reasonably

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<sup>41</sup>See *id.* at 571.

<sup>42</sup>See *id.* at 566.

<sup>43</sup>See *Polubinski, Closing the Channels of Communication*, *supra* note 25, at 1025.

<sup>44</sup>*Central Hudson*, 447 U.S. at 563.

<sup>45</sup>*In re RMJ*, 455 U.S. 191, 203 (1982). Because inherently misleading speech carries substantial social harms, and the state obviously has a compelling interest in preventing such harms, speech that is inherently misleading may be regulated on that basis alone. See *id.*

<sup>46</sup>See *Polubinski, Closing the Channels of Communication*, *supra* note 25, at 1025, citing *Peel v. Attorney Registration and Disciplinary Commission of Illinois*, 496 U.S. 91, 100 (1990) quoting *In re RMJ*, 455 U.S. at 203.

<sup>47</sup>See *Central Hudson*, 447 U.S. at 563.

<sup>48</sup>*Friedman v. Rogers*, 440 U.S. 1, 13 (1979).

<sup>49</sup>See *In re RMJ*, 455 U.S. 191.

related to a substantial governmental interest?<sup>50</sup> On several occasions, the Supreme Court has held that a government's "interest in promoting the health, safety, and welfare of its citizens... provide[s] a sufficiently 'substantial' governmental interest to justify regulation."<sup>51</sup> In addition, the Court has noted that the government's interest in "ensuring the accuracy of commercial information in the marketplace is substantial."<sup>52</sup> Consequently, the government often asserts as its substantial interests public safety and health and protection from economic adulteration.

The third factor asks whether the regulation at issue directly advances the government interest asserted.<sup>53</sup> More specifically, such a regulation "may not be sustained if it provides only ineffective or remote support for the government's purpose."<sup>54</sup> The Court has picked up the anti-paternalistic theme from *Virginia Pharmacy* and *Bates* here. In a more recent decision, the Court again noted that a paternalistic motive will not suffice: "A State's paternalistic assumption that the public will use truthful, nonmisleading commercial information unwisely cannot justify a decision to suppress it."<sup>55</sup>

Finally, the Court will evaluate the fit between the government's ends and the means chosen to accomplish those ends. In *Central Hudson*, this was a "not more extensive than is necessary" test.<sup>56</sup> Post-*Central Hudson* cases watered down this requirement. In *Fox*, the Court refused to invalidate a university's rule prohibiting commercial enterprises from operating in campus facilities as a *per se* violation, reformulating the fourth prong of the *Central Hudson* standard.<sup>57</sup> The Court explained that the *Central Hudson* test does not impose a "least restrictive means" requirement, but only mandates a "reasonable" fit "that represents

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<sup>50</sup>See *Central Hudson*, 447 U.S. at 566.

<sup>51</sup>*Rubin v. Coors Brewing Co.*, 514 U.S. 476, 485(1995) *citing* *Posadas de Puerto Rico Assocs. v. Tourism Co. of Puerto Rico*, 478 U.S. 328, 341 (1986).

<sup>52</sup>*Edenfield v. Fane*, 507 U.S. 761 (1993).

<sup>53</sup>See *Central Hudson*, 447 U.S. at 566.

<sup>54</sup>*Central Hudson*, 447 U.S. at 564. The government must "demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree." *Edenfield*, 507 U.S. at 770-771.

<sup>55</sup>*44 Liquormart v. Rhode Island*, 517 U.S. 484, 497 (1996) (Stevens, J. writing the plurality opinion). "The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good." *Id.* at 503.

<sup>56</sup>*Central Hudson*, 447 U.S. at 566.

<sup>57</sup>See *Board of Trustees of the State University of New York v. Fox*, 492 U.S. 469, 480 (1989).



not necessarily the single best disposition but one whose scope is in proportion to the interest served.”<sup>58</sup>

Although the 1980s witnessed a less stringent standard of scrutiny for restrictions on commercial speech,<sup>59</sup> the 1990s proved to be an era of relative invigoration of the commercial speech doctrine.<sup>60</sup> The biggest change in the commercial speech doctrine landscape occurred with the Supreme Court’s analysis in *44 Liquormart v. Rhode Island*.<sup>61</sup> In the wake of the case, a statute or regulation appears to face a greater burden the more the state aims its restrictions at noncommercial aspects of commercial speech.<sup>62</sup> The Court addressed a challenge by licensed liquor retailers to a Rhode Island statute prohibiting advertising of alcohol price information.<sup>63</sup> The Court unanimously agreed that the statute violated the First Amendment, although the case produced a web of concurrences. Writing for a plurality of four, Justice Stevens condemned the “wholesale suppression of truthful, nonmisleading information”<sup>64</sup> and rejected the proposition that commercial speech in areas of heavy regulation enjoys no First Amendment protection. Justice Thomas went even further, calling for the abolition of the *Central Hudson* test and substitution of *per se* invalidity in the case of such paternalistic restrictions.<sup>65</sup> On the other hand, Justice O’Connor, writing for four justices, found Rhode Island’s fit unreasonable under a more cautious reading of *Central Hudson* than the vigorous version advanced by Justice Stevens.<sup>66</sup> The decision heralded a more protective attitude toward commercial speech<sup>67</sup>: no special category of unprotected commercial speech exists for labeling and other communications and one author comments that, read together, the opinions of Justices Stevens, Scalia, and Thomas suggest that

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<sup>58</sup>*Id.* at 480. *The regulation in question does not have to be the “absolute least restrictive means to achieve the desired end.” Id.* at 476-477. See also *Edenfield*, 507 U.S. at 762 (the means must advance the objective in a “direct and material way.”)

<sup>59</sup>See Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 64.

<sup>60</sup>See *id.* at 69.

<sup>61</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1015.

<sup>62</sup>See *id.* at 1019.

<sup>63</sup>See 517 U.S. at 489-492.

<sup>64</sup>*Id.* at 505 (Stevens, concurring). See also Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 72.

<sup>65</sup>See Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 72, discussing *44 Liquormart*, 517 U.S. at 518, 526-528 (Thomas, J., concurring).

<sup>66</sup>Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 72.

<sup>67</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 72.

the Court would consider restrictions on a manufacturer's communications more critically under the *Central Hudson* test than it would other restrictions on commercial speech because of the significant informational character of such communications.<sup>68</sup>

## B. Defining Commercial Speech

Author Nat Stern notes that, although no rules exist for defining the contours of the commercial speech category, certain themes and decisions have been sufficiently definite to form a discernible picture of what expression the Supreme Court is likely to regard as commercial speech.<sup>69</sup> In determining whether to invoke the limited protection afforded "commercial speech," the earliest cases addressing the issue focused on whether the speech at issue did "no more than propose a commercial transaction."<sup>70</sup> This sort of speech appears to bear what the Court regarded as the hallmarks of commercial speech: objectivity and hardiness.<sup>71</sup> While continuing to affirm simple proposals of commercial transactions as falling within the "core notion of commercial speech," the Court has also suggested that the category encompasses a larger sphere of expression.<sup>72</sup> In *Friedman*, the Court treated trade names as commercial speech because the expression could reasonably be linked to a proposal to buy or sell.<sup>73</sup> In *Central Hudson*, the Court declared a distinction between fully protected "direct comments on public issues" and statements "made only in the context of commercial transactions."<sup>74</sup>

The Court's approach to expression containing a mixture of commercial and non-commercial elements was refined in two major decisions addressing the problem of classification: *Bolger v. Young's Drug Products*

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<sup>68</sup>See *id.* at 1022.

<sup>69</sup>See Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 79. See also Murphy, "It's Time to Make a Good Agency Better," *supra* note 9. The Supreme Court has not agreed on precisely how "commercial speech" should be defined, addressing in depth the definition of commercial speech in only one case. See *id.*

<sup>70</sup>*Virginia Pharmacy*, 425 U.S. at 762, *quoting* *Pittsburgh Press Company v. Human Relations Commission*, 413 U.S. 376, 385 (1973). See also Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1016.

<sup>71</sup>See Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 79.

<sup>72</sup>See *id.* at 80.

<sup>73</sup>See *id.* *Friedman*, 440 U.S. at 11.

<sup>74</sup>*Central Hudson*, 447 U.S. at 563.

*Corporation* and *Fox*.<sup>75</sup> In *Bolger*, the Supreme Court addressed for the first time whether the speech at issue was “pure speech,” entitled to full protection of the First Amendment, or “commercial speech,” entitled to only more limited protection.<sup>76</sup> At issue were flyers and informational pamphlets that described the benefits and availability of condoms. Because the pamphlets contained discussions of important public issues as well as descriptions of condoms manufactured by Youngs, the Court conceded that the pamphlets transcended simple proposals of commercial transactions.<sup>77</sup> Consequently, the Court cited three factors that influenced its decision that the communication at issue was commercial speech: (1) the speech was concededly an advertisement; (2) the speech referred to a specific product; and (3) the speaker had an economic motivation for disseminating the speech.<sup>78</sup> Noting that none of the factors is determinative, the Court has made clear that the existence of an underlying profit motive does not by itself operate to remove full First Amendment protection.<sup>79</sup> The *Bolger* Court noted that a company has the option of addressing public issues directly if it wants full First Amendment protection.<sup>80</sup> In *Fox*, the Supreme Court adopted a similar focus, noting that the non-commercial portion of the hybrid speech could be expressed elsewhere.<sup>81</sup> At issue were banned “Tupperware parties,” which consisted of a sales pitch and discussion of topics such as financial and domestic responsibility.<sup>82</sup> The Court observed that the admittedly non-commercial component of the expression was not essential to the central purpose of the presentations.<sup>83</sup> Consequently, the Court reviewed the university’s

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<sup>75</sup>See Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 81.

<sup>76</sup>See Murphy, “It’s Time to Make a Good Agency Better,” *supra* note 9, at —. The Supreme Court has not agreed on precisely how “commercial speech” should be defined, addressing in depth the definition of commercial speech in only one case. See *Bolger v. Youngs Drug Products Corp.*, 463 U.S. 60 (1983). The material was sent out by the manufacturer in the form of a mass mailing to the public. The U.S. Postal Service notified the manufacturer that the mailing violated a federal law and the manufacturer brought the case seeking a declaratory judgment. The Court ruled that a statute which prohibited the mailing of advertisements for contraceptives violated the manufacturer’s First Amendment commercial speech rights. See *id.* at 61, 67.

<sup>77</sup>See *Bolger*, 463 U.S. at 66, 68.

<sup>78</sup>See *id.* at 66-67.

<sup>79</sup>See *id.* The Court noted that none of these factors is either necessary or sufficient for a determination of whether the speech at issue is commercial speech. See *id.* See also Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1016, citing *Fox*, 492 U.S. at 482; *Virginia Pharmacy*, 425 U.S. at 761.

<sup>80</sup>See Stern, *In Defense of the Imprecise Definition of Commercial Speech*, *supra* note 26, at 82.

<sup>81</sup>See *id.*

<sup>82</sup>See *id.*

<sup>83</sup>See *id.*

regulations under the standard for commercial speech.<sup>84</sup> Thus, regulatory and legislative provisions challenged under the commercial speech doctrine will face a reinvigorated analysis under the traditional *Central Hudson* standard.

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<sup>84</sup>See *id.*

## II. Three Landmark Cases

### A. Washington Legal Foundation v. Henney: Challenge to FDA's Policy Regarding Certain Off-Label P

#### 1. *Background on Off-Label Promotion Through Enduring Materials and CME Seminars*

Traditionally, under the FD&C Act, a manufacturer could not promote a product for any use other than the ones for which the company received FDA approval. Before a manufacturer can lawfully market a prescription drug, FDA must approve the product for both safety and efficacy.<sup>85</sup> Alternative uses for approved drugs, or off-label uses, are subjected to the same FDA review procedures as the initial claim.<sup>86</sup> Consequently, in 1992, FDA published a “Draft Policy Statement on Industry-Supported Scientific and Educational Activities.”<sup>87</sup> The notice explains that FDA has traditionally viewed scientific and educational activities sponsored by the companies that market the products involved as “labeling,” but the draft guideline clarifies that FDA does not wish to regulate these activities if they are truly independent from manufacturer influence and are non-promotional.<sup>88</sup> On October 8, 1996, FDA published two additional draft guidance documents, “Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data” and “Guidance for Industry-Funded Dissemination of Reference Texts.” FDA essentially limited manufacturers to dissemination of peer-reviewed journal articles that discuss those adequate and well-controlled clinical trials that were relied upon by FDA in approving the product for the intended use. Similarly, FDA allowed dissemination of medical texts by manufacturers, even where the texts discussed off-label use if the texts were prepared independently of the manufacturer’s interests, did not focus primarily on any particular product,

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<sup>85</sup>See 21 U.S.C. § 355(a)-(b) (1994); 21 C.F.R. §§ 314.50, 314.100 (1996).

<sup>86</sup>See 21 U.S.C. § 321(p). In 1962, Congress amended the definition of “new drug” to make clear that drugs must be demonstrated safe and effective for “use under the conditions prescribed,” meaning that all uses for a drug must obtain FDA approval. See *Washington Legal Foundation v. Friedman*, 13 F.Supp.2d 51, 55 (D.D.C. 1998) (hereinafter “WLF I”).

<sup>87</sup>57 Fed. Reg. 56,412 (Nov. 27, 1992).

<sup>88</sup>Id. See also *Murphy*, “It’s Time to Make a Good Agency Better,” *supra* note 9, at 605.

and did not focus primarily on an off-label use. In addition, the text must not have been written, edited, or significantly influenced by the product manufacturer. Although FDA received comments from various groups contesting the constitutionality of these policies,<sup>89</sup> FDA published the Final Guidance Documents with the same basic guidelines.<sup>90</sup> In addressing the comments received, FDA firmly restated its conviction that a very broad definition of “labeling” brings industry-supported scientific and educational activities that involve the sponsoring company’s product well within FDA jurisdiction.<sup>91</sup>

Despite the limitations on a manufacturer’s ability to promote unapproved uses, off-label use is an important part of medical practice.<sup>92</sup> Doctors and researchers discover new uses for drugs which are not described in the product’s labeling, meaning that the uses differ from those tested and approved by FDA. FDA does not attempt to regulate the prescription of products for unapproved uses.<sup>93</sup>

## 2. WLF Court Finds Guidance Documents Unconstitutional

In 1994, the Washington Legal Foundation (WLF) brought a lawsuit challenging the Guidance Documents discussed above,<sup>94</sup> seeking to enjoin FDA and the Department of Health and Human Services from enforcing policies restricting certain forms of manufacturer promotion of off-label uses for FDA-approved drugs and

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<sup>89</sup>WLF provided feedback to FDA in response to the agency’s request for comments, noting its First Amendment freedom of speech concerns with certain policies.

<sup>90</sup>See *Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data* (61 Fed. Reg. 52,800 (Oct. 1996)); *Guidance for Industry Funded Dissemination of Reference Texts* (61 Fed. Reg. 52,800 (Oct. 1996)); and *Final Guidance on Industry Supported Scientific and Educational Activities* (62 Fed. Reg. 64,074) (FDA set forth twelve factors that would be considered in determining whether the activity is independent from the influence of the manufacturer).

<sup>91</sup>See Murphy, “It’s Time to Make a Good Agency Better,” *supra* note 9, at 605, citing 62 Fed. Reg. at 64,075. Consequently, the final versions of the Guidance Documents were basically the same as the Draft Documents.

<sup>92</sup>Off-label use is very common across medical specialties and may constitute the best treatment for many patients in varied circumstances. Forty-four of 36 approved anti-cancer drugs are used for at least one off-label indication. See Sarah F. Jagger, Director of Health Services Quality and Public Issues, GAO, Statement before the Sept. 1996 House Hearing (Sept. 12, 1996); 1996 WL 10830746, at \*3.

<sup>93</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 992. See also 59 Fed. Reg. 59820, 59821 (1994) (noting that the agency has restated this policy on numerous occasions).

<sup>94</sup>WLF specifically challenged the policies discussed in note 91.

devices.<sup>95</sup> The threshold question for the court is how to classify the speech at issue. FDA argues that the speech regulated by the Guidance Documents falls outside the ambit of the First Amendment because of the federal government's extensive power to regulate the pharmaceutical industry.<sup>96</sup> The court notes that this argument does not comport with current First Amendment jurisprudence, and that the speech is afforded some type of constitutional protection.<sup>97</sup> WLF argues that the speech was scientific and academic speech, entitled to the highest level of First Amendment protection. FDA argues, on the other hand, that the Guidance Documents were incidental encroachments upon speech and entirely compatible with the First Amendment. In the alternative, FDA claims that the Guidance policies at most regulate commercial speech.<sup>98</sup>

In analyzing whether the speech at issue is "pure speech" or "commercial speech," the court notes that the resolution of the question is not an easy one because the communications present one of those "complex mixtures of commercial and non-commercial elements."<sup>99</sup> The application of the three *Bolger* factors directs the conclusion that both types of communication are properly classified as commercial speech.<sup>100</sup> Typical commercial speech is uttered directly by the commercial entity that wishes to financially benefit from the message. Here, however, the speech manufacturers wish to communicate is the speech of others. WLF argues that, although the manufacturer may have an economic motivation, that is insufficient, without more, to transform enduring materials and Continuing Medical

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<sup>95</sup>See *WLF I*, 13 *F.Supp.* at 54.

<sup>96</sup>See *id.* at 60.

<sup>97</sup>See *id.* at 60, discussing 44 *Liquormart*, 517 U.S. at – (rejecting the concept that, because the government has the power to regulate extensively in a certain area, the government also has the authority to regulate speech without raising First Amendment concerns).

<sup>98</sup>See *id.* at 59.

<sup>99</sup>*Id.* at 62, quoting *Bolger*, 463 U.S. at 81 (*Stevens, J. concurring*).

<sup>100</sup>See note 79 and accompanying text. The WLF court also relies on an analogy to *Bolger* to bolster its conclusion. Among the informational pamphlets that Youngs Drug Products Company wished to mail included one entitled "Plain Talk About Venereal Disease," which discussed condom use without any specific reference to the varieties manufactured by the company. The court still concluded that the pamphlet constituted commercial speech. See *Bolger*, 463 U.S. at 67. The court notes that in the instant case, although one could argue that the reprints and seminars are merely informational, because the information is in fact supplied by the manufacturer, and because the primary purpose is to encourage the purchase of the featured product, the speech is commercial speech. See *id.*

Education (CME) seminars into commercial speech.<sup>101</sup> The court determines that the drug manufacturers endeavor to disseminate enduring materials and sponsor CME seminars in order to increase the sales volume of their drugs and that therefore the speech is commercial in nature.<sup>102</sup>

After determining that the communication involved is commercial speech, the court uses the *Central Hudson* standard to evaluate the constitutionality of the Guidance Documents. Notably, the Court rejects FDA's position that all unapproved speech is inherently misleading:

In asserting that any and all scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs are preemptively untruthful or misleading until the FDA has had the opportunity to evaluate them, FDA exaggerates its overall place in the universe.<sup>103</sup>

Deciding that the Guidance Documents address speech that is directed toward lawful activity and that is not misleading, the court concludes that the first prong of the test is satisfied.<sup>104</sup> The court next addresses the second inquiry: whether the interest asserted by the government is substantial. The court rejects the first asserted interest, that of ensuring that physicians receive accurate and unbiased information so that they can make informed prescription decisions, as overly paternalistic.<sup>105</sup> The court notes that physicians are capable of critically evaluating journal articles or textbook reprints or the findings presented at CME seminars.<sup>106</sup> However, the court finds that the government's interest in providing manufacturers with ample incentive to get previously unapproved uses approved to be substantial.<sup>107</sup>

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<sup>101</sup>See *id.* at 62, relying on *Bolger*, 463 U.S. at 67.

<sup>102</sup>See *id.* at 64. One author has argued that the speech in the enduring materials (peer-reviewed journal articles and reference texts) should be classified pure speech rather than commercial speech. See Murphy, "It's Time to Make a Good Agency Better," *supra* note 9, at 621. Using the *Bolger* analysis, she argues that (1) enduring materials are not necessarily advertisements; (2) enduring materials do not always mention the "product name"; and most important, (3) plaintiffs who invoke their right to receive the enduring materials may have no economic motivation at all. See *id.*

<sup>104</sup>See *id.* at 69.

<sup>105</sup>See *id.* See also notes 28 & 55 and accompanying text.

<sup>106</sup>See *id.* at 70.

<sup>107</sup>See *id.* at 69. FDA focused on the harm that may come to patients if off-label uses become prevalent before adequate and well-controlled clinical trials are conducted by manufacturers and assessed by FDA. See *id.* at 71. WLF



Requiring manufacturers to submit supplemental applications to obtain approval for new uses directly advances the substantial government interest.<sup>108</sup> However, the Guidance Documents fail to meet the fourth factor and are therefore unconstitutional. The restrictions are more extensive than necessary to encourage manufacturers to get new uses on-label.<sup>109</sup> The District Court therefore holds that WLF is entitled to judgment as a matter of law<sup>110</sup> and issues an injunction.<sup>111</sup> The Court notes that FDA may still sanction the dissemination of any material that is false or misleading.<sup>112</sup> Moreover, FDA can require pharmaceutical manufacturers to disclose an interest in drugs or devices and the fact that the use discussed has not been approved by FDA.<sup>113</sup>

### 3. WLF Court Reevaluates First Amendment Doctrine After the Enactment of FDAMA

Following the enactment of FDAMA, the District Court denied FDA's motion to confine the application of the injunction to the express provisions of the Guidance Documents, and proceeded to evaluate whether the changes in FDA policy effected by FDAMA brought FDA into compliance with the First Amendment.<sup>114</sup>

For the first time in recent years, drug manufacturers were permitted by statute to engage in the off-label

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*focused on the harm that may come to patients, especially in the field of orthopedics and oncology, if the information does not reach the health care provider. See id. at 72. See also Murphy, "It's Time to Make a Good Agency Better," supra note 9, at 609.*

<sup>108</sup>See WLF I, 13 F.Supp.2d at 71.

<sup>109</sup>See *id.* at 73. The court notes that the determination was based in large part because a less-burdensome alternative exists: full and complete disclosure. See *id.*

<sup>110</sup>See *id.* at 62, 65, 73. See also Elizabeth A. Weeks, *Is It Worth the Trouble? The New Policy on Dissemination of Information on Off-label Drug Use Under the Food and Drug Modernization Act*, 54 FOOD & DRUG L.J. 645, 649 (1999).

<sup>111</sup>The Court held that the FDA shall not in any way prohibit, restrict, sanction or otherwise seek to limit any pharmaceutical or medical device manufacturer or any other person from: disseminating peer-reviewed articles, regardless of its proposing off-label uses and regardless of whether the articles mentions the original FDA-approved study; disseminating reference textbooks published by a bona fide independent publisher regardless of whether it proposes off-label uses; and suggesting content/speakers at a symposium regardless of off-label promotion. See WLF I, 13 F.Supp.2d at 73. See also *Washington Legal Foundation v. Friedman*, 36 F.Supp.2d 16 (D.D.C. 1999) (hereinafter "WLF II") (redline amended order granting summary judgment and permanent injunction.

<sup>112</sup>See WLF II, 36 F.Supp.2d at 419.

<sup>113</sup>See *id.*

<sup>114</sup>See *Washington Legal Foundation v. Henney*, 56 F.Supp.2d 81 (D.D.C. 1999) (hereinafter "WLF III").

marketing and promotion of drugs and devices, subject to a variety of legislative constraints.<sup>115</sup>

The court holds that FDAMA unconstitutionally restricted protected commercial speech.<sup>116</sup> As with the Guidance Documents, the Court applies the four-factor *Central Hudson* test. The court again concludes that the speech is neither unlawful nor inherently misleading.<sup>117</sup> Similarly, the Court finds that FDA does have a substantial interest—that of encouraging manufacturers to seek FDA approval of off-label uses.<sup>118</sup> However, the Court determines that only one of the policies contained in the provisions of FDAMA at issue directly advances that substantial government interest—the supplemental application.<sup>119</sup> Nevertheless, the Court finds that the supplemental application requirement was unconstitutional because it fails to satisfy the means-ends test. The application burdens substantially more speech than necessary.<sup>120</sup> Consequently, the court amends the injunction to enjoin the FDAMA provisions at issue.<sup>121</sup> Thus, the decision in *WLF* provided FDA with its first direct warning that over-regulation of commercial speech could infringe on those rights guaranteed by the First Amendment.<sup>122</sup>

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<sup>115</sup>See *Salbu*, *Off-Label Use*, *supra* note 5, at 212. Section 401 of FDAMA adds a new subchapter D to the FD&C Act, consisting of new sections 551-557, authorizing manufacturers to disseminate information on unapproved uses of approved drugs, biological products, and devices. The provisions represent a compromise; they allow distribution, but only if the manufacturer complies with a number of restrictions. Section 551 permits a manufacturer to distribute written information concerning an off-label use if, *inter alia*, the information is not derived from research conducted by another manufacturer, without its permission; the manufacturer submits the information to FDA sixty days before beginning distribution, together with safety and effectiveness information from clinical trials and safety information from reports of clinical experience; and the manufacturer includes a prominent statement that the use has not been approved, a copy of the approved labeling, and disclosures relating to authorship and funding. Under § 552, manufacturers may only disseminate information in the form of (1) an unabridged peer-review article published on a scientific or medical journal about a “scientifically sound” clinical investigation; or (2) a reference publication containing similar information. To qualify, the reference publication must not have been prepared at the manufacturer’s request, significantly influenced or distributed solely by the manufacturer, focus on a particular drug or device, or present materials that are false or misleading. Finally, in order to disseminate such information, § 554 requires a manufacturer to submit to FDA a supplemental application covering the new use, certify that it will submit such a supplement, or seek an exemption within six months of the initial dissemination of information under § 551.

<sup>116</sup>See *WLF III*, 56 F.Supp.2d at 82. The court held that 21 U.S.C. §§ 360aaa-360aaa-6 was unconstitutional insofar as it was inconsistent with the injunctive provision. See *id.* at 88.

<sup>117</sup>See *id.* at 85.

<sup>118</sup>See *id.* at 86.

<sup>119</sup>See *id.* at 86-87.

<sup>120</sup>See *id.* at 87.

<sup>121</sup>See *id.* at 87-88. Note that FDA appealed the District Court’s conclusion. The Court of Appeals held that the appeal would be dismissed for lack of constitutional controversy, where FDA took the position on appeal that FDAMA did not provide it with independent authority to proscribe speech and *WLF* responded that it no longer had a constitutional objection to FDAMA or FDA. See *Washington Legal Foundation v. Henney*, 202 F.3d 331 (D.C. Cir. 2000) (*hereinafter* “*WLF IV*”).

<sup>122</sup>See Steven B. Steinborn and Kyra A. Todd, *The End of Paternalism: A New Approach to Food Labeling*, 54

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*Background on Health Claims*

For over fifty years, FDA has vigorously regulated nutritional claims by dietary supplements under both the food and drug provisions of the FD&C Act.<sup>123</sup> FDA established detailed labeling requirements for foods marketed for “special dietary uses” shortly after the enactment of the 1938 Act.<sup>124</sup> After FDA concluded that it needed stricter requirements to control the claims made for vitamin-mineral products, the Agency published new regulations in 1966.<sup>125</sup> The new regulations were immediately challenged, leading eventually to a court decision that in 1974 invalidated and remanded to the Agency for further consideration several portions of the rules.<sup>126</sup> In 1976, Congress intervened, amending the FD&C Act to limit FDA's regulatory authority and enforcement power in relation to vitamin and mineral supplements.<sup>127</sup> Consequently, FDA was temporarily prevented from extensively regulating the composition of dietary supplements.

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*FOOD & DRUG L.J.* 401, 409 (1999).

<sup>123</sup>See *FOOD & DRUG LAW*, *supra* note 1, at 207. See also Melinda Ledden Sidak, *Dietary Supplements and Commercial Speech*, 48 *FOOD & DRUG L.J.* 441 (1993). FDA can regulate a food as a drug depending on the nature of the claims made because FD&C Act defines drugs to include “articles intended for use in diagnosis, cure, mitigation, treatment or prevention of disease and articles (other than food) intended to affect the structure of any function of the body.” 21 U.S.C. § 321(g) (FD&C Act § 201(g)). The “other than food” exception has been narrowly construed by FDA. See Sidak, *Dietary Supplements*, at 441.

<sup>124</sup>See David F. Cavers, *The Food, Drug, and Cosmetic Act of 1938: Its Legislative History and its Substantive Provisions*, *FOOD & DRUG LAW*, *supra* note 1, at 212. For example, the original 1941 regulations for vitamin and mineral supplements required that their labels declare the percent of the minimum daily requirement contained in each recommended amount. See *id.* See also Sidak, *Dietary Supplements*, *supra* note 124, at 442.

<sup>125</sup>See Cavers, *The Food, Drug, and Cosmetic Act of 1938*, *FOOD & DRUG LAW*, *supra* note 1, at 212; See also Sidak, *Dietary Supplements*, *supra* note 124, at 442, discussing 31 Fed. Reg. 8521 (June 18, 1966).

<sup>126</sup>See Sidak, *Dietary Supplements*, *supra* note 124, at 442, discussing *National Nutritional Foods Ass'n v. FDA*, 504 F.2d 761 (2<sup>nd</sup> Cir. 1974).

<sup>127</sup>See *id.* at 443, citing Pub.L. No. 94-278, § 501, 90 Stat. 401, 410-13 (1976). Section 411 prohibits FDA from imposing maximum limits of vitamins and mineral potencies for other than safety reasons, classifying as a drug any vitamin or mineral solely because it exceeds the potency limits recommended by FDA, and limiting the combination or number of any safe vitamin, mineral, or other food ingredients in vitamin and mineral supplements. See *FOOD & DRUG LAW*, *supra* note 1, at 221. While constricting FDA authority with respect to regulating the composition of dietary supplements, the 1976 law gave the agency limited authority to regulate the advertising of dietary foods. This new authority was considered by some as compensation for the loss of FDA's authority over vitamin and mineral supplements' composition. See *id.*

Passage of the Nutritional Labeling and Education Act of 1990 (NLEA), however, gave FDA the impetus to renew its regulatory efforts.<sup>128</sup> The NLEA creates an explicit exception to the general prohibition of drug-like claims by authorizing FDA to pre-approve “health claims” that are supported by “significant scientific agreement.”<sup>129</sup> In 1994, the legitimacy of structure/function claims for foods was also enhanced by the enactment of DSHEA.<sup>130</sup> Nevertheless, FDA has had a restrictive implementation,<sup>131</sup> and one author argues that the NLEA has not fostered the broad dissemination of health claims or other diet and health information that many groups had hoped.<sup>132</sup>

In order to assert health claims for conventional foods, the NLEA provides that products must obtain prior FDA authorization.<sup>133</sup> The Secretary will approve the claim only if she determines that there is “significant scientific agreement” among qualified experts that the claim is supported by the totality of publicly available scientific evidence.<sup>134</sup> Congress adopted a slightly different approach for evaluating health claims for dietary supplements. Instead of mandating a particular standard, Congress delegated to FDA the task of developing a procedure and standard for such health claims.<sup>135</sup> FDA published a proposed rule in the Federal Register, planning to adopt the same standard for dietary supplements that Congress had already adopted for foods in conventional form. Although FDA received comments challenging the “significant scientific agreement” standard, the Agency adopted the standard in its final rule.

## 2. *District Court in Pearson Finds that Policies Withstand Constitutional Scrutiny*

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<sup>128</sup>See Sidak, *Dietary Supplements*, *supra* note 124, at 443. The NLEA’s purpose is to regulate more strictly the kind of claims that can be made in food labeling, including dietary supplements. See *id.*

<sup>129</sup>21 U.S.C. § 343(r). See also Steinborn, *The End of Paternalism*, *supra* note 123, at 403.

<sup>130</sup>See Steinborn, *The End of Paternalism*, *supra* note 123, at 403. The net effect of the DSHEA and NLEA is that structure/function claims are permissible. See *id.*

<sup>131</sup>See *id.* at 406.

<sup>132</sup>See *id.* at 408. “The restrictive approach of NLEA and FDA’s cautious interpretation of its authority denied consumers’ access to widely available diet/health information on food labels.” *Id.*

<sup>133</sup>See 21 U.S.C. § 343(r)(3)(B)(i).

<sup>134</sup>*Id.*

<sup>135</sup>See *id.*

Manufacturers, distributors, and organizations of consumers of dietary supplements brought suit challenging both the general rule issued by FDA for determining the validity of health claims for dietary supplements, as well as four separate regulations addressing claims for specific disease-nutrient relationships, issued pursuant to that general rule.<sup>136</sup> Pearson and other dietary supplement manufacturers had requested unsuccessfully, in part, that FDA approve the manufacturers' proposed claims with qualifications that would reflect the shortcomings in the science found by FDA.<sup>137</sup> The District Court found that neither the "significant scientific agreement" standard for Dietary Supplements, nor the refusal to allow the health claims violates the First Amendment.<sup>138</sup>

The court uses the four-part *Central Hudson* standard to reach its conclusion. The court begins its discussion by dismissing the plaintiffs' contention that the "significant scientific agreement" standard is overbroad and a prior restraint on commercial speech.<sup>139</sup> FDA argues that any health claim which cannot meet the "significant scientific agreement" standard is misleading to consumers, and in particular, as applied to the four health claims at issue. The failure to meet the standard makes the claims misleading because they

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<sup>136</sup>See *Pearson v. Shalala*, 14 F.Supp.2d 10, 13 (D.D.C. 1998) (hereinafter "*Pearson I*").

<sup>137</sup>See *Pearson I*, 14 F.Supp.2d at 14. See also Steinborn, *The End of Paternalism*, *supra* note 123, at 410. Plaintiffs argued that dietary supplements should not be subject to the same procedure and standard as conventional foods. Plaintiffs also objected to the FDA's proposed denial of the specific health claims they wanted to place on the labels of dietary supplements. In particular, plaintiffs sought permission for the following health claims on dietary supplement labels: (1) "Consumption of antioxidant vitamins may reduce the risk of certain kinds of cancers"; (2) "Consumption of dietary fiber may reduce the risk of colorectal cancer"; (3) "Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease"; (4) "The U.S. Public Health Service has estimated that fifty percent of neural tube defects may be averted annually if all women maintained an adequate intake of folate during childbearing years"; and (5) ".8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in food in common form." See *Pearson I*, 14 F.Supp.2d at 410. Note that the plaintiffs' claim on folate and neural tube defects became moot on April 19, 1996, when FDA issued a Final Rule which eliminated the restriction on the use of the Public Health Service Statement, provided that the statement was accompanied with additional information noting that the claim is population-based. See 61 Fed.Reg. 8752, 8775-8776, 8781.

<sup>138</sup>See *Pearson I*, 14 F.Supp.2d at 17.

<sup>139</sup>See *id.* at 18. The court notes that the Supreme Court has held that the overbreadth analysis does not apply to commercial speech. See *id.* discussing *Fox*, 492 U.S. at 481. The court also notes that there is no case law holding that the prior restraint doctrine is applicable to commercial speech. See *id.* at 18.

have not been scientifically validated.<sup>140</sup> The court agrees with this argument, holding that a statement is inherently misleading when “the particular method by which the information is imparted to consumers is inherently conducive to deception and coercion.”<sup>141</sup> The court notes that the public lacks the necessary knowledge to evaluate the health claims when not subject to reliable verification through the consumer’s personal experience.<sup>142</sup> Consequently, the court determines that FDA has satisfied the *Central Hudson* test for both the “significant scientific agreement” standard and the four rejected health claims.<sup>143</sup>

On the chance that a court could determine that the health claims language is only partially misleading, the court evaluates the plaintiffs’ claims under the remaining *Central Hudson* factors.<sup>144</sup> The court finds that the government has a substantial interest in protecting the health and safety of consumers.<sup>145</sup> Moreover, it determines that the regulation directly advances the government interest asserted in preventing consumer fraud by unsupported health claims.<sup>146</sup> Finally, the court finds that the regulation is no more extensive than necessary to serve the government’s interest.<sup>147</sup> FDA’s objective is to protect consumer health and well being by preventing the dissemination of unsupported or insubstantial scientific information on dietary supplement labeling. The regulation is sufficiently narrowly tailored by Congress to affect only the label itself or materials directly attached to the label of the dietary supplement. As such, the regulation is no broader than necessary to protect the public health and prevent consumer fraud.<sup>148</sup> Finding that the defendant has satisfied the *Central Hudson* test, the District Court dismisses the action for failure to state a claim.<sup>149</sup>

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<sup>140</sup>See *id.* at 18.

<sup>141</sup>*Id.* at 18, quoting *Peel*, 496 U.S. at 112.

<sup>142</sup>See *id.* at 18.

<sup>143</sup>See *id.* at 19.

<sup>144</sup>See *id.*

<sup>145</sup>See *id.*

<sup>146</sup>See *id.* at 20. The court refers to the inability of consumers to do research and analyze often conflicting scientific studies to determine whether a health claim is valid. See *id.*

<sup>147</sup>See *id.*

<sup>148</sup>See *id.* at 20.

<sup>149</sup>See *id.* The court also addressed the plaintiffs’ non-First Amendment concerns. The court found that the “significant scientific agreement” standard for dietary supplements does not violate the Fifth Amendment for vagueness. See *id.* at 21. The court also concluded that the “significant scientific agreement” standard does not violate the NLEA, or the Administrative Procedure Act. See *id.* at 14-17.

### 3. Appellate Court Determines that Policies are Unconstitutional

On appeal, the D.C. Circuit concludes that the proposed health claims are *not* inherently misleading, unlike the lower court, and that FDA is required under the commercial speech doctrine to consider whether inclusion of appropriate disclaimers could negate the potentially misleading nature of health claims.<sup>150</sup>

As below, FDA attempts to preclude analysis under the commercial speech doctrine, arguing that manufacturers do not enjoy the First Amendment rights to free speech when FDA deems the “speech” in violation of FD&C Act.<sup>151</sup> The Court rejects FDA’s argument, finding the contention “almost frivolous,”<sup>152</sup> and proceeds to analyze the restrictions under the *Central Hudson* standard.<sup>153</sup> FDA argues that even if the claims are only potentially misleading,<sup>154</sup> under *Central Hudson*, the government is not obliged to consider requiring disclaimers in lieu of an outright ban on all claims that lack “significant scientific agreement.”

<sup>155</sup> The court disagrees, finding that disclaimers are constitutionally preferable to outright suppression of

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<sup>150</sup>See *Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999) (hereinafter “*Pearson II*”). The court also disagreed with the lower court’s ruling under the Administrative Procedure Act (APA), finding that FDA’s failure to define the phrase “significant scientific agreement” in regulation governing authorization of health claims violated the APA. See *id.* The D.C. Circuit later rejects FDA’s suggestion for rehearing en banc. See *Pearson v. Shalala*, 172 F.3d 72 (D.C. Cir. 1999) (hereinafter “*Pearson III*”). Judge Silberman, concurring in the denial of rehearing, noted that the government cannot advance a major nonjurisdictional argument for the first time at the rehearing stage. FDA argued that neither employing a health claim as a trigger to the drug approval process nor subjecting “drugs” to the drug approval process raises a First Amendment concern. This was an attempt at a “greater includes the lesser” argument. See *id.*

<sup>151</sup>See Steinborn, *The End of Paternalism*, *supra* note 123, at 409, discussing 58 Fed. Reg. at 2526-27. As below, the Agency contended that health claims lacking “significant scientific agreement” are inherently misleading and thus outside the protection of the First Amendment. 164 F.3d at —. “Inherently misleading advertising may be prohibited entirely.” *In re R.M.J.*, 455 U.S. 191, 203 (1982).

<sup>152</sup>*Peel v. Attorney Registration and Disciplinary Commission of Illinois*, 496 U.S. 91, 105 (1990) (rejecting paternalistic assumption that the recipients of a letterhead are “no more discriminating than the audience for children’s television”).

<sup>153</sup>*Pearson II*, 164 F.3d at 655, discussing *Bolger*, 463 U.S. at 67-68.

<sup>154</sup> “[T]he states may not place an absolute prohibition on...potentially misleading information...if the information may also be presented in a way that is not deceptive.” *In re R.M.J.*, 455 U.S. at 203.

<sup>155</sup>See *Pearson II*, 164 F.3d at 658. The court focused its analysis on whether it is permissible for FDA to prohibit potentially misleading speech rather than allow speech with adequate qualifications. See *id.*

commercial speech.<sup>156</sup>

The court agrees with the analysis of the District Court, finding that FDA has asserted a substantial governmental interest: the protection of public health<sup>157</sup> and the prevention of consumer fraud.<sup>158</sup> After evaluating whether the regulation directly advances the government interest asserted, however, the court determines that the protection of public health is too paternalistic. Thus, only the prevention of consumer fraud stands as a legitimate interest advanced by the regulatory scheme. As in *WLF*, FDA stumbled on the last factor of the *Central Hudson* test: the court finds that the fit between the government's ends and the means chosen to accomplish those ends is not "reasonable."<sup>159</sup> The court holds that the preferred remedy is more disclosures rather than less.<sup>160</sup>

The Court does not conclude, however, that all claims may be made truthful by the inclusion of a disclaimer; instead it defers to FDA's determination of whether a claim is so misleading that it could not be rendered nonmisleading by a disclaimer.<sup>161</sup> Consequently, the message of *Pearson* is that FDA may not prohibit commercial speech if there are less restrictive ways in which the message can be presented that ensure the claim will not mislead consumers.<sup>162</sup> FDA retains the legal authority to prohibit false or misleading labeling claims, but *Pearson* now requires FDA to consider whether and how such information can be presented to consumers in a way that informs without misleading.<sup>163</sup> The net effect is intended to ensure that FDA

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<sup>156</sup>See *id.* at 658.

<sup>157</sup>The government has a substantial interest in "promoting the health, safety, and welfare of its citizens." Rubin, 514 U.S. 476.

<sup>158</sup>"There is no question that [the government's] interest in ensuring the accuracy of commercial information in the marketplace is substantial." Edenfield, 507 U.S. 761.

<sup>159</sup>See *Pearson II*, 164 F.3d at 657, citing *Fox*, 492 U.S. 469 (discussing *Central Hudson*, 447 U.S. at 564-66). The court found that FDA had failed to meet the fourth requirement of the *Central Hudson* test. See *id.* The Supreme Court explained in *Fox* that the *Central Hudson* test does not impose a "least restrictive means" requirement, but only mandates a "reasonable fit" between means and ends. *Fox*, 492 U.S. at 480.

<sup>160</sup>See *Pearson II*, 164 F.3d at 658, discussing *Bates*, 433 U.S. at 376. Disclaimers are preferable to outright suppression. See, e.g., *Peel*, 496 U.S. at 110; *In re R.M.J.*, 455 U.S. at 206; *Shapiro v. Kentucky Bar Association*, 486 U.S. 466, 478 (1988).

<sup>161</sup>See Steinborn, *The End of Paternalism*, *supra* note 123, at 411 discussing *Pearson II*, 164 F.3d at 659.

<sup>162</sup>See *id.*

<sup>163</sup>See *id.*



adopt sufficiently flexible policies that foster the broad dissemination of useful information to consumers.<sup>164</sup> Thus, the importance of the case goes far beyond the facts of *Pearson* because FDA’s approach in *Pearson* is merely illustrative of FDA’s view of its authority in the numerous contexts in which it is charged with protecting consumers.<sup>165</sup>

### C. Western States Medical Center v. Shalala: Challenge to FDA’s Policy Forbidding Advertising

#### 1. *Background on Compounded Drugs*

As noted, the FD&C Act imposes stringent conditions on the manufacture and distribution of new drugs.<sup>166</sup> All new drugs must comply with the requirements of the Act unless Congress has provided an explicit exemption. Historically, while FDA has subjected new drugs to its requirements, it has permitted pharmacists to compound drugs without meeting these stringent safety standards. Compounding is the process by which a pharmacist combines, mixes, or alters ingredients to create a medication that serves the unique needs of specific patients. Consequently, prior to the enactment of FDAMA in 1997, FDA had never exercised its authority to subject compounded drugs to the FD&C Act’s requirements. Nevertheless, FDA had expressed concern about the manufacture of new drugs under the guise of compounding.<sup>167</sup> In a Compliance Policy Guidance, FDA set forth nine factors the Agency would use to determine whether a drug provider’s efforts to produce a particular drug justified FDA’s exercise of enforcement action under the FD&C Act.<sup>168</sup> In 1997, Congress formally recognized this policy in FDAMA. Section 127 of FDAMA added a new § 503A to the FD&C Act, permitting pharmacies to compound drugs under specified circumstances.<sup>169</sup> Under subsection

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<sup>164</sup>See *id.*

<sup>165</sup>See *id.*

<sup>166</sup>See 21 U.S.C. § 355(a).

<sup>167</sup>See *Compliance Policy Guidance from 1992*.

<sup>168</sup>See *id.*

<sup>169</sup>See 21 U.S.C. § 503A. The section provides that a drug product may be compounded without complying with the requirement for GMPs, adequate directions for use, or NDA approval if it is compounded by a licensed pharmacist or physician for an identified individual patient based on the unsolicited receipt of a valid prescription that a compounded

(a), the drug product must be compounded “for an identified individual patient based on the unsolicited receipt of a valid prescription order.”<sup>170</sup> Subsection (b) imposes numerous standards on the quality of the ingredients of the compounded drug, requiring *inter alia*, that the drug product be compounded from a list of approved drug substances that have not been deemed unsafe or inappropriate for compounding.<sup>171</sup> Finally, under subsection (c), a drug may be compounded “only if the pharmacy, licensed pharmacist or licensed physician does not advertise or promote the compounding of any particular drug, class or drug, or type of drug.”<sup>172</sup>

## 2. *WSMC v. Shalala*<sup>173</sup>

Pharmacists brought an action challenging subsections (a) and (c).<sup>174</sup> Because the parties agree that the speech implicated by these sections is limited to commercial speech, the court uses the *Central Hudson* standard to evaluate the limitations placed on the pharmacists’ compounding services and ability to advertise those services.<sup>175</sup> The court concludes that the speech targeted by the restrictions at issue is not “inherently misleading.”<sup>176</sup> The court notes that FDA has presented no evidence that the prohibited statements contain false information and finds the unsupported assertion that the public will be misled into believing by implication alone, that compounded drugs have passed FDA tests and been approved, insufficient to warrant the conclusion that the restricted speech is inherently misleading.<sup>177</sup> Moreover, the court notes that

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*drug is necessary for the patient. See also Summary of FDAMA, supra note 11, at 44.*

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<sup>174</sup>Subsection (a) required that a prescription for the particular compounded drug be unsolicited and that it be prepared for an identified patient and §(c) required that the drug may be compounded only if the pharmacy does not advertise or promote the compounding of any particular drug, class of drug, or type of drug. See § 353(a) & (c) of FDAMA.

<sup>175</sup>See *WSMC*, 69 *F.Supp.2d* at 1297.

<sup>176</sup>See *id.* at 1298-99.

<sup>177</sup>See *id.* The court points out a legitimate example of regulation where an advertisement was misleading. See *U.S. v. An Article... Acu-Dot*, 483 *F.Supp.* 1311 (N.D. Ohio 1980). There, the defendants were manufacturers of a “small, pin-head sized magnet attached to the underside of a circular, adhesive patch,” which was designed to work as a minor pain reliever. Defendants marketed the product as useful for temporary relief of occasional minor aches and pains of muscles and joints. FDA brought suit against the defendants, claiming that the product had only a placebo

the potentially misleading element can be reduced by the use of a narrower restriction, such as a disclaimer on advertisements indicating that FDA approval has not been obtained.<sup>178</sup> The court concludes, therefore, that the speech at issue is not inherently misleading and may not be prohibited without reference to the remaining *Central Hudson* factors.<sup>179</sup>

FDA posits three substantial interests: (1) the general goal of protecting the public health and safety<sup>180</sup>; (2) the integrity of the drug approval process<sup>181</sup>; and (3) the interest in balancing the continued availability of compounded drug products as a component of individualized drug therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding.<sup>182</sup> While the court agrees that the first two asserted interests are substantial, it finds the third interest insufficiently clear.<sup>183</sup> The court notes that it cannot agree with FDA that the government has a substantial interest in achieving some amorphous and imprecise balance between the availability of compounded drugs and the prevention of disguised manufacturing.<sup>184</sup>

The court next examines whether the provisions of FDAMA directly advance the two legitimate governmental interests asserted. FDA argues that the speech-related restrictions limit the volume of compounded

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*effect, and therefore, the defendants' promotional statements about the product were misleading. The defendants did not dispute that the drugs had only a placebo effect, but contended that the placebo effect was sufficient to warrant the defendants' claims regarding the drug's health benefits. The court disagreed. On these facts, the court held that the marketer's claim that the device itself provided temporary relief of minor aches and pains was false, and thus also misleading. See id.*

<sup>178</sup>See *WSMC*, 69 F.Supp.2d at 1300, citing *Peel*, 496 U.S. 91. In *Peel*, the Attorney Registration and Disciplinary Commission of Illinois brought disciplinary proceedings against the plaintiff under a rule prohibiting attorneys from representing themselves to the public as specialists. See *Peel*, 496 U.S. 91. The plaintiff attorney had obtained a "Certificate in Civil Trial Advocacy" from the National Board of Trial Advocacy and noted that on his letterhead. See *id.* The Commission asserted that the plaintiff thereby implied to the public that he was a certified legal specialist. See *id.* The Supreme Court explained that a state may prohibit inherently misleading speech entirely, but it cannot impose an absolute prohibition if the information may be presented in a non-misleading manner. See *id.* The Court recommended that as an alternative to a broad prohibition, the defendants could require a disclaimer to ensure that complete information about attorneys' qualifications was provided to the public. See *id.* It could not, however, broadly proscribe truth information whose negligible misleading content could be remedied by providing more information. See *id.* See also *Virginia Pharmacy*, 425 U.S. at 772; *Nutritional Health Alliance v. Shalala*, 953 F.Supp. 526, 528 (S.D.N.Y. 1997).

<sup>179</sup>See *WSMC*, 69 F.Supp.2d at 1301.

<sup>180</sup>See *id.* at 1301.

<sup>181</sup>See *id.* at 1302.

<sup>182</sup>See *id.* at 1302.

<sup>183</sup>See *id.* at 1301-1302.

<sup>184</sup>See *id.* at 1303.

drugs, thereby ostensibly protecting the public against purported health risks. The court finds that the government fails to draw the necessary connection between the asserted interests and restricting the volume of compounded drugs,<sup>185</sup> referring to the *Pearson* decision.<sup>186</sup> Moreover, the court notes that other courts have considered and flatly dismissed the government’s argument, rejecting the “paternalistic” view that suppression of truthful speech is necessary to protect physicians and consumers from their own misuse of truthful information.<sup>187</sup> The court also determines that § 353a of FDAMA does not directly advance the asserted governmental interest of preserving the integrity of the FDA approval process,<sup>188</sup> finding that, if this were truly FDA’s concern, the Agency could require that all drugs, including compounded drugs, obtain prior FDA approval.<sup>189</sup> Thus, the statute fails to satisfy the third prong of the *Central Hudson* standard. The court notes that, even if it were to conclude that the statute could satisfy the “directly advance” requirement, the statute is flawed because it fails under the fourth factor.<sup>190</sup>

The court determines that the restriction is more extensive than necessary to achieve the asserted government interest.<sup>191</sup> The court again notes that FDA could rely on disclaimers, similar to the suggestion in *Pearson*. Alternatively, the court reminds FDA that the Agency could subject compounded drugs to the safety testing imposed on new drugs,<sup>192</sup> rather than broadly prohibiting truthful speech.<sup>193</sup>

<sup>185</sup>See *id.* at 1304. See also *Central Hudson*, 447 U.S. at 566 (the court examines whether the regulation at issue “directly advances the state interest involved”). Under this test, the regulation “may not be sustained if it provides only ineffective or remote support for the government’s purpose.” See *id.* Rather, to satisfy this requirement, “the government must demonstrate that its restrictions will in fact alleviate [the asserted harms] to a material degree.” *Valley Broadcasting Co. v. U.S.*, 107 F.3d 1328, 1334 (9<sup>th</sup> Cir. 1997), quoting *Edenfield*, 507 U.S. at 769. The government must meet its burden in a direct and material way. See *Edenfield*, 507 U.S. at 767. The government body must “demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree.” *Id.* at 770-771.

<sup>186</sup>See *WSMC*, 69 F.Supp.2d at 1304.

<sup>187</sup>See, e.g., *WLF I*, 13 F.Supp.2d 51; see also *Virginia Pharmacy*, 425 U.S. 748. In *Virginia Pharmacy*, the Supreme Court struck down a Virginia statute prohibiting pharmacists from advertising their prices for prescription drugs. See *id.* In reaching its conclusion, the court expressed its aversion to the use of suppression as a means to prevent “uninformed” individuals from misusing accurate information. See *id.*

<sup>188</sup>See *WSMC*, 69 F.Supp.2d at 1306.

<sup>189</sup>See *id.*

<sup>190</sup>See *id.* at 1307.

<sup>191</sup>See *id.* at 1307.

<sup>192</sup>See *id.* at 1308.

<sup>193</sup>See *id.* at 1309. The court denies the defendant’s motion for summary judgment and grants the plaintiffs’ cross-motion for summary judgment, enjoining DFA from enforcing the speech-related restrictions contained in §§

## IV. Evaluation of Other FDA Policies Restricting Off-Label Promotion

After the assault on FDA policies and federal law, which led to a declaration of the violation of manufacturers’ First Amendment freedom of speech rights, FDA will face increased pressure from consumers and manufacturers to expand access to information and the ability to promote unapproved uses of prescription drugs and medical devices.

A.

### Background

#### 1. *Labeling*

The FD&C Act gives FDA jurisdiction over the labeling of prescription and non-prescription drugs and restricted medical devices. The Act’s definitions of “label” and “labeling” apply to drugs and devices without differentiation.<sup>194</sup> The term “label” applies only to what is affixed to the container that holds the actual product.<sup>195</sup> “Labeling,” however, has a much broader definition.<sup>196</sup> It is generally understood to include any written material that supplements or explains the product, is disseminated by the manufacturer, and reaches the customer, doctor, or patient either before, with, or after the product.<sup>197</sup> As part of the application for approval of a new drug or device, the manufacturer must submit the proposed final labeling

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353a(a) and (c). See *id.* at 1310.

<sup>194</sup>See *FOOD & DRUG LAW*, *supra* note 1, at 397.

<sup>195</sup>See 21 U.S.C. § 321(k) (“a display of written, printed, or graphic material upon the immediate container of any article”).

<sup>196</sup>See 21 U.S.C. § 321(m). “Labeling” includes “all labels and other written, printed or graphic” material on or “accompanying” a product. *Id.*

<sup>197</sup>See Edward M. Basile, Ellen Armentrout, and Kelly N. Reeves, *Medical Device Labeling and Advertising: An Overview*, 54 *FOOD & DRUG L.J.* 519, 519 (1999), discussing *U.S. v. Urbeteit*, 335 U.S. 355 (1948) (holding descriptive leaflets constituted labeling even though the shipment of leaflets did not accompany shipment of devices).

for the product.<sup>198</sup> In general, labeling must not be false or misleading in any particular,<sup>199</sup> must provide adequate directions for use,<sup>200</sup> and must contain adequate warnings when the drug may be dangerous to health if used in certain pathological conditions or in unsafe dosages or methods of duration of administration or application.<sup>201</sup> Labeling can be false or misleading even if not technically false or literally untrue.<sup>202</sup> One court expanded the definition of “misleading” to include instances when the total effect of the labeling is to deceive or mislead.<sup>203</sup> Consequently, manufacturers must present a “fair balance” of information relating to side effects and the effectiveness of the product.<sup>204</sup> In addition, any required labeling statements must be placed on the label “with such conspicuousness (as compared with other words, statements, designs, or devices in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.”<sup>205</sup> FDA will approve the application only if the labeling is acceptable and conforms precisely with the uses for which the Agency has found the product to be effective.<sup>206</sup> If the labeling of a drug includes unapproved indications, it will be deemed misbranded.<sup>207</sup> FDA’s general rule with regard to medical devices is, similarly, that medical device firms are not permitted to promote devices if they are not approved or cleared. FDA “approves” pre-market approval applications, but only “clears” 510(k) submissions. FDA’s regulations prohibit the use of “approved” with respect to a 510(k) clearance because it implies that the clearance is a finding of the safety and effectiveness of the device,

<sup>198</sup>See *Polubinski, Closing the Channels of Communication*, *supra* note 25, at 995, discussing 21 U.S.C. § 355(b)(1)(F) and 21 C.F.R. § 314.50(e)(2)(ii).

<sup>199</sup>See *id.* at 54, FN 34.

<sup>200</sup>See 21 U.S.C. § 352(a). A drug or device is misbranded if the label is false or misleading. See *id.*

<sup>201</sup>See David W. Opderbeck, *How Should FDA Regulate Prescription Drug Promotion on the Internet?*, 53 *FOOD & DRUG L.J.* 47, 54 (1998), citing 21 U.S.C. § 352(f).

<sup>202</sup>See *Basile, Medical Device*, *supra* note 198, at 521.

<sup>203</sup>See *U.S. v. One Device, More or Less, Ellis Micro-Dynameter*, 224 F.Supp. 265 (E.D. Pa. 1963).

<sup>204</sup>See *Basile, Medical Device*, *supra* note 198, at 521.

<sup>205</sup>See Opderbeck, *How Should FDA Regulate Prescription Drug Promotion*, *supra* note 202, at 54, citing 21 U.S.C. § 352(c).

<sup>206</sup>See *Polubinski, Closing the Channels of Communication*, *supra* note 25, at 995. See also 21 U.S.C. § 331(a) and (d). FDA will approve the application only if the labeling is acceptable and conforms with the uses for which it has found the product to be effective. See *id.*

<sup>207</sup>See Marilyn A. Moberg, James W. Wood, and Howard L. Dorfman, *Surfing the Net in Shallow Waters: Product Liability Concerns and Advertising on the Internet*, 53 *FOOD & DRUG L.J.* 213, 215 (1998).

whereas it is only a conclusion of “substantial equivalence.”<sup>208</sup> A device is approved for marketing based on its “intended use,” where “intended use” refers to the “objective intent of the persons legally responsible for the labeling of devices.”<sup>209</sup> Regulations further provide that intended use may be shown:

if the article is, with the knowledge of the persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised. . . [I]f a manufacturer knows, or has knowledge of facts that would give him notice that a device introduced into interstate commerce by him is to be used for conditions, purposes, or other uses than the ones for which he offers it, he is required to provide adequate labeling for such a device which accords with such other uses to which the article is to be put.<sup>210</sup>

Under §205(b) of FDAMA, FDA’s determination of the intended use, for purposes of determining substantial equivalence, shall be based upon the proposed labeling submitted in the 510(k). If FDA thinks that off-label use is likely, the Agency can require an appropriate statement in the labeling. However, FDA cannot refuse to clear the device for marketing based on concerns about potential harms from the unlabeled use.<sup>211</sup>

FDA has issued warning letters for violations of the rule restricting promotion of unapproved uses for approved or cleared devices. For instance, FDA sent a warning letter to a company that had a device cleared under § 510(k) for “the local administration of ionic drug solutions into the body for medical purposes and [for use] as an alternative to injections.”<sup>212</sup> The sponsor was promoting the device for use with a specific drug without FDA approval of the drug for iontophoretic administration.<sup>213</sup> An exception to the general prohibition of unapproved/uncleared use promotion is the Investigation Device Exemption.<sup>214</sup> FDA permits manufacturers of Class III investigational devices to distribute “Notices of Availability of an Investigational Device” to recruit investigators for clinical studies.<sup>215</sup> However, the manufacturer must not state, suggest, or

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<sup>208</sup>21 C.F.R. § 807.97.

<sup>209</sup>21 C.F.R. § 801.4.

<sup>211</sup>See *Summary of FDAMA*, *supra* note 11, at 61.

<sup>212</sup>See *Basile, Medical Device*, *supra* note 198, at 526, discussing *Letter from Lillian J. Gill, Director, Office of Compliance, CDRH to Empi, Inc. (Aug. 31, 1999)*.

<sup>213</sup>See *id.*

<sup>214</sup>See *id.* at 525.

<sup>215</sup>Guidance for Industry and FDA Staff: Preparing Notices of Availability of Investigational Medical Devices and for Recruiting Study Subjects (Mar. 19, 1999).

imply that the investigational device is safe or effective for its investigational indication.<sup>216</sup> If a drug or device is not labeled properly, or “misbranded,” it is subject to seizure by FDA.<sup>217</sup> Consequently, manufacturers are prohibited from putting unapproved uses on the labeling of drugs or devices.

## 2. *Advertising*

Until 1962, the Federal Trade Commission controlled all food, drug, and cosmetic advertising. The 1962 amendments to the FD&C Act changed that.<sup>218</sup> Now, FDA has authority to regulate all drug labeling and prescription drug advertising. FTC, however, retains authority to regulate advertising of non-prescription drugs.<sup>219</sup> An “advertisement” is defined by FDA to include “advertisements in published journals, magazines, other periodicals, and newspapers, and advertisements broadcast through media such as radio, television, and telephone communications systems.”<sup>220</sup> While advertisements, unlike labels, may not require full disclosure, they must be balanced, cannot be misleading, and must include core information on major side effects and contraindications. While FDA will review advertising at the request of the company, it does not require preclearance of advertising, unlike with labeling.<sup>221</sup>

The requirements for advertising a drug or medical device are detailed in the FD&C Act. Note that there is no clear distinction between advertising and labeling, and many advertisements will meet the definition of labeling and can be regulated as such.<sup>222</sup> Consequently, FDA regulates medical device advertising in various ways—either it meets the definition of labeling, or FDA will regulate advertising for restricted devices or statements regarding the intended use of a device. FDA does not have authority to regulate advertising for 510(k)-cleared devices unless the device has been deemed restricted by regulation or the advertising also constitutes labeling or relates to intended use.<sup>223</sup> Medical device advertising must contain: the “established” name of the product in at least half the size of the trade name; a

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<sup>216</sup>See *id.*

<sup>217</sup>See 21 U.S.C. §§ 301, 331-332, 334, 352.

<sup>218</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at —.

<sup>219</sup>See 21 U.S.C. § 502(n).

<sup>220</sup>21 C.F.R. § 201(1)(1)(1996).

<sup>221</sup>See Moberg, *Surfing the Net*, *supra* note 208, at 216.

<sup>222</sup>See Basile, *Medical Device*, *supra* note 198, at —.

<sup>223</sup>See *id.* at 520.



brief statement of the intended uses and warnings, precautions, side effects and contraindications; and when needed, a description of the device's components.<sup>224</sup> Advertisements of prescription drugs must contain: the "established" name of the product in type at least half the size as that used for the trade or brand name; the formula showing quantitatively each ingredient of such drug to the extent required for the labels under section 352(e); and such other information "in brief summary" relating to side effects, contraindications, and effectiveness.<sup>225</sup> Regulations in this area are extensive, requiring a lengthy and detailed list of information about the advertised product in the "brief summary" that must accompany the ad.<sup>226</sup> In addition to these requirements, the regulations state that advertisements must reflect "fair balance," cannot promote unapproved uses,<sup>227</sup> cannot omit material information so as to be misleading, and cannot make comparative claims involving a competitor's product without "substantial" evidence from two well-controlled trials to support the claim.<sup>228</sup> FDA looks not only at the advertisement's actual language, but also the "theme" and "form."<sup>229</sup>

Nevertheless, FDA has initiated changes over the past few years that have dramatically broadened the ways in which drug manufacturers advertise pharmaceutical products directly to consumers.<sup>230</sup> Today, pharmaceutical companies place advertisements on television, radio, and the Internet, for the first time directly informing patients about the purposes, functions, and advantages of various prescription drug products.<sup>231</sup> One author notes that, although FDA continues to fight what it regards as abusive practices, its general tendency has been toward relaxation rather than enhanced control.<sup>232</sup> Despite this "relaxation" and the decision in *WLF* permitting manufacturers to engage in limited dissemination of information about off-label uses, the communication of unapproved uses directly to consumers remains prohibited. An ad may not differ materially from the information in the brief summary, which in turn must

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<sup>224</sup>See 21 U.S.C. § 352(r).

<sup>225</sup>See *id.* § 352(n).

<sup>226</sup>21 C.F.R. § 202.1(e).

<sup>227</sup>See Moberg, *Surfing the Net*, *supra* note 208, at 216.

<sup>228</sup>See *id.*

<sup>229</sup>See *id.*

<sup>230</sup>See Salbu, *Off-Label Use*, *supra* note 5, at 185.

<sup>231</sup>See *id.* at 185.

<sup>232</sup>See *id.*

conform to the product's labeling<sup>233</sup> (*i.e.*, no unapproved uses).

Broadcast advertisements must contain the brief summary unless “adequate provision is made for dissemination of the approved or permitted package labeling in connection with the broadcast presentation.”<sup>234</sup> Practically speaking, the brief summary is essentially the same as the prescribing information required under the labeling regulations.<sup>235</sup> “Reminder advertisements” are exempted from the brief summary requirement.<sup>236</sup> “Reminder advertisements” are those “which call attention to the name of the drug product but do not include indications or dosage recommendations for use of the drug product.”<sup>237</sup> They need only contain the drug's proprietary and established name, the established name of each active ingredient, and other optional information.<sup>238</sup> As the discussion of current labeling and advertising law reveals, FDA restricts manufacturer's ability to discuss and promote all potential uses of their drugs and devices. In the current environment of encouraging increased consumer access to information and reliance on the use of disclaimers as an alternative to broad suppression of speech, FDA may not be able to contain off-label promotion. The paper evaluates promotion of unapproved uses in the context of labeling, DTC advertisements, and the Internet. Each analysis considers arguments for the proper categorization of the speech and the proper outcome under the relevant First Amendment doctrine.

B.

#### Restriction on promoting unapproved uses on the labeling of prescription drugs and medical d

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<sup>233</sup>See 21 C.F.R. § 202.1(e). See also Basile, *Medical Device*, *supra* note 198, at 528. After WLF, a manufacturer may still not advertise off-label uses for previously approved products directly to the consumer. See *id.* at 528.

<sup>234</sup>Opderbeck, *How Should FDA Regulate Prescription Drug Promotion*, *supra* note 202, at 55, *quoting* 21 C.F.R. § 202.1(e).

<sup>235</sup>See *id.* at 55.

<sup>236</sup>See *id.*, *citing* 21 C.F.R. § 202.1(e)(2)(i).

<sup>237</sup>See *id.*

<sup>238</sup>See *id.* at 55-56.

The regulations which prohibit manufacturers from discussing unapproved uses of their products on labels or labeling is a restrictive policy, which might come under attack, much as the restrictive policies regarding dissemination of information about off-label uses in *WLF*. The analysis will be conducted as though drug manufacturers have sued FDA because they want to put information about an unapproved on the label or labeling of the product. As in *WLF*, FDA would likely argue that its policies are only “incidental encroachments upon speech.”<sup>239</sup> FDA has long taken the position that the labeling of a prescription drug is fully regulable and that its controls therefore raise no First Amendment concerns.<sup>240</sup> For FDA, drug labeling has long constituted a separate area of speech in which extensive regulation is permissible.<sup>241</sup> Moreover, the Agency’s interpretation finds at least tacit support from the courts. In *Kordel v. United States*, the Supreme Court endorsed FDA’s broad definition of drug and device labeling.<sup>242</sup> Consequently, FDA has argued that labeling occupies a “distinct category” of speech subject to a more generous analysis.<sup>243</sup> This argument is likely to fail, however, because of the Supreme Court’s decision in *Liquormart*. In *Liquormart*, the Court rejected the notion that, where the government has extensive power to regulate, it has the authority to regulate speech without raising First Amendment concerns.<sup>244</sup> Just as the District Court in *WLF* refused to permit regulation of speech merely because the federal government has extensive power to regulate the pharmaceutical industry, a court would likely reject the argument in the context of pure labeling control as well. Polubinski concurs, noting that, under current commercial speech jurisprudence, no such separate category of non-regulable speech exists.<sup>245</sup>

After determining that the activity at issue is speech rather than conduct, a court would need to determine whether

<sup>239</sup>*WLF I*, 13 F.Supp.2d at 59.

<sup>240</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1013, citing David G. Adams, *FDA Policy on Industry-Supported Scientific and Educational Activities: Current Developments*, 47 *FOOD & DRUG L.J.* 629, 1414-16 (1992).

<sup>241</sup>See *id.* FDA has suggested that food labeling restriction receive more “limited scrutiny” than is “afforded restrictions on speech under extensive regulatory schemes involving areas of economic activity.” See *id.* at 1013-14.

<sup>242</sup>See *Kordel v. U.S.*, 333 U.S. 345 (1948).

<sup>243</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1014. See also *Ohralik*, 436 U.S. at 456. The *Ohralik* Court stated, “Numerous examples could be cited of communications that are regulated without offending the First Amendment, such as the exchange of information about securities, corporate proxy statements, the exchange of price and production information among competitors, and employer’s threats of retaliation for the labor activities of employees.” *Id.*

<sup>244</sup>44 *Liquormart*, 517 U.S. at ---. See also *WLF I*, 13 F.Supp.2d at 60, discussing 44 *Liquormart*, 517 U.S. at ---.

<sup>245</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1014.

labeling represents pure speech, entitled to full First Amendment protection, or commercial speech, entitled to more limited protection.<sup>246</sup> Much like the speech at issue in *Bolger* and *Fox*, the speech here has both commercial and non-commercial components. Using the *Bolger* factors, a court could analyze the label and labeling and the proposed placement of unapproved uses. Is the speech concededly an advertisement?<sup>247</sup> Polubinski argues that labeling has a promotional objective, particularly within the Supreme Court’s conception of advertising.<sup>248</sup> In determining the scope of the FC&C Act’s conception of labeling, the *Kordel* court explained: “Every labeling is in a sense an advertisement.”<sup>249</sup> A product’s labeling does seek to influence physicians in their choice on which drug to prescribe.<sup>250</sup> Consequently, although product labeling does serve an important informational public health function, it also satisfies the first *Bolger* prong because it is also partly advertising.<sup>251</sup> Second, the speech by design refers to a specific product.<sup>252</sup>

Finally, a court will consider the third *Bolger* factor: whether the speaker has an economic motivation for disseminating the speech.<sup>253</sup> Manufacturers are motivated at least in part by economic interest. A drug or device manufacturer’s central concern is selling the product and it will fashion its label accordingly, to the extent FDA will permit.<sup>254</sup> As in *WLF*, this factor is potentially troublesome because of the dual role of the speech: it is both informational and commercial.<sup>255</sup> One author notes that, as with the first factor, the analysis under the third factor is complicated by the fact that at least some labeling does serve other functions. However, he notes that, if anything, the informational component would indicate that pure labeling might be entitled to greater protection than commercial speech.<sup>256</sup>

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<sup>246</sup>See note -- and accompanying text.

<sup>247</sup>See *Bolger*, 436 U.S. at —.

<sup>248</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1016.

<sup>249</sup>*Kordel*, 335 U.S. at 351. See also U.S. v. 24 Bottles Sterling Vinegar and Honey, Etc., 338 F.2d 157, 159 (2<sup>nd</sup> Cir. 1964) (holding that, in the context of promotion of “Folk Medicine[,]...advertising and labeling overlap; most labels advertise as well”).

<sup>250</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1016.

<sup>251</sup>See *id.* at 1016-1017.

<sup>252</sup>See *Bolger*, 436 U.S. at —. See also Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1017. The pure labeling of prescription drugs plainly refers to a specific product. See *id.*

<sup>253</sup>See *Bolger*, 436 U.S. at —.

<sup>254</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1017.

<sup>255</sup>See *WLF I*, 13 F.Supp.2d at —, discussing *Bolger*, 436 U.S. at 81.

<sup>256</sup>See Polubinski, *Closing the Channels of Communication*, *supra* note 25, at 1017.

Plaintiffs opposing FDA's regulations would use that idea, arguing as did the plaintiff in *WLF* that, although the manufacturer may have an economic motive, that is insufficient without more to transform the label into commercial speech.<sup>257</sup> Nevertheless, as did the *WLF* court, a court would likely decide that the manufacturer is sufficiently motivated by economic motives. A court would likely be reinforced in its decision because the speech at issue (off-label uses on the label and labeling) is the manufacturer's own, not that of another party which the manufacturer is disseminating. Consequently, unapproved uses on-label would be considered commercial speech.<sup>258</sup>

Next, a court would turn to the *Central Hudson* standard, applying the four factors as they have evolved in subsequent cases. The purpose here is to evaluate whether FDA's tight restrictions on valid label information restricts a manufacturer's right to commercial speech. The first factor evaluates whether the speech is inherently misleading and thus outside First Amendment protection.<sup>259</sup> If the manufacturer wishes to put unapproved uses on its labeling, the FDA will likely argue that the speech is inherently misleading, as it did in *WLF*. Regulations are intended to ensure that labeling contains accurate and complete information regarding approved use and risks.<sup>260</sup> Whereas the court in *WLF* rejected the argument that all unapproved speech is inherently misleading, a court would need to consider the truth of the information and its ability to mislead. Unapproved uses listed on a label could be true and verifiable facts. The question is whether a potential customer could be actually misled or deceived by a label with unapproved uses listed. The Supreme Court in *Peel* considered the public's ability to evaluate an attorney's listing of certifications and noted that potential legal clients can understand that licenses in general are issued by governmental authorities, whereas a host of certificates are issued by private organizations. The Court held that the public will not be misled by the designation of "certified."<sup>261</sup> Will consumers similarly understand the listing of unapproved uses on-label? It depends in large part whom one perceives the consumers (i.e., the recipients of the commercial speech)

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<sup>257</sup>See *WLF*, 13 F.Supp.2d at 62. A plaintiff would want to keep the speech under the "pure speech" heading in order to ensure full First Amendment protection.

<sup>258</sup>Cf. Polubinski, *Closing the Channels of Communication*, supra note 25, at 1013. Polubinski notes that under the Supreme Court's commercial speech jurisprudence, pure labeling would likely constitute commercial speech. *Id.*

<sup>259</sup>See note -- about RMJ and accompanying text.

<sup>260</sup>See *Salbu*, *Off-Label Use*, supra note 5, at 187.

<sup>261</sup>See *Peel*, 496 U.S. at 104.

to be. In *WLF*, the recipients were clearly physicians, whom the court thought capable of evaluating information and making informed decisions. If a court thinks that, similarly, the “consumer” here is physicians, then there will be less of a problem. Although the ultimate goal is consumer protection, prescription drug labels today are aimed at physicians, who act as “learned intermediaries” between manufacturers and users.<sup>262</sup> However, if the consumer is determined to be the public at large, we might question whether the public is likely to be deceived. Although more than just the unapproved use would be required in the labeling (warnings, precautions, clinical pharmacology, etc. for unapproved uses would be required in the labeling), the question remains whether the public at large can evaluate such detailed and scientific information. In *Pearson*, the court rejected such an argument with respect to health claims for dietary supplements, noting that courts have rejected a paternalistic motive on the part of the government.<sup>263</sup> Dietary supplements are subject to much less stringent regulation than prescription drugs, however. A court would have to weigh the interest in the information versus the “possibilities for deception.”<sup>264</sup> The court’s decision under this factor would be a much closer call than in *WLF*. The decisions in *WLF*, *Pearson*, and *WSMC* should signal, however, that increased consumer access to information is a legitimate right that cannot be stifled under paternalistic motives.

If a court were to decide that the speech the manufacturer wishes to place on the label were merely potentially misleading, the court would proceed with the remaining *Central Hudson* factors.<sup>265</sup> The plaintiff would argue that, at most, the unapproved use is potentially misleading, and would rely on the Supreme Court’s analysis in *In re R.M.J.*: “...the state may not place an absolute prohibition on certain types of potentially misleading information... if the information also may be presented in a way that is not deceptive.”<sup>266</sup> FDA will assert that the government’s restriction is reasonably related to a substantial interest.<sup>267</sup> The asserted interest would likely revolve around public health

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<sup>262</sup>See *Salbu*, *Off-Label Use*, *supra* note 5, at 187.

<sup>263</sup>See *Pearson II*, 164 F.3d at ---.

<sup>264</sup>*In re R.M.J.*, 455 U.S. at ---.

<sup>265</sup>“Even when a communication is not misleading, the state retains some authority to regulate.”’ *In re R.M.J.*, 455 U.S. at 203.

<sup>266</sup>*Id.* at 203.

<sup>267</sup>See *Central Hudson*, 447 U.S. at 566.

and safety as well as protection from economic fraud.<sup>268</sup> If the manufacturer seeks to place unapproved uses on the drug’s label, FDA will likely offer similar arguments as it did in *WLF*: the government has an interest in the provision of accurate and unbiased information to physicians (and end-consumers) as well as an incentive to get unapproved uses formally approved.<sup>269</sup> FDA has a stronger argument here than it did in *WLF*. Generally, in enduring materials, the context of the unapproved use will be provided, *e.g.*, the clinical trial and the complete results. Moreover, the “speaker” is not the manufacturer *per se*, as in the labeling context. Although physicians are capable of critically evaluating journal articles or textbook reprints,<sup>270</sup> they would have a much harder time evaluating the merits of an unapproved use advocated by the manufacturer. Manufacturers’ reliance on previous cases’ disdain for paternalistic motives might not carry its argument here. As the Supreme Court noted in *Edenfield*, there is no question that a state’s interest in “ensuring the accuracy of commercial information in the marketplace is substantial.”<sup>271</sup> Consequently, a court might find that FDA has asserted a legitimate government interest in assuring accurate and unbiased information. As for the second asserted interest, providing an incentive to get unapproved uses formally approved, the court would likely find it legitimate, as the District Court did in *WLF*.

That the government’s asserted interests are substantial in the abstract does not mean that its blanket prohibition on unapproved uses on labels and labeling serves those interests.<sup>272</sup> The party seeking to “uphold a restriction on commercial speech carries the burden of justifying it.”<sup>273</sup> Moreover, the government body seeking to sustain a restriction on commercial speech must demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree.<sup>274</sup> The regulations prohibiting the placement of unapproved uses in labeling do directly advance both interests. By preventing drug manufacturers from including unapproved uses on a drug’s label, the manufacturer will be forced to use other routes to inform physicians of unapproved uses. These routes are

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<sup>268</sup>See footnotes -- and --- and accompanying text.

<sup>269</sup>See *WLF I*, 13 *F.Supp.2d* at 69.

<sup>270</sup>See *id.* at 70.

<sup>271</sup>*Edenfield*, 507 U.S. at 769.

<sup>272</sup>Cf. *id.* at 770.

<sup>273</sup>*Bolger*, 463 U.S. at 770.

<sup>274</sup>See *Edenfield*, 507 U.S. at 770-771, citations omitted.

probably more conducive to complete explanations, review by others in the field, information on clinical trials, etc. In addition, drug manufacturers will be forced to seek FDA approval in order to get new uses on-label.<sup>275</sup>

Thus, a court will turn to an examination of the means and ends. Because commercial speech is linked inextricably with the commercial transaction it proposes, the state's interest in regulating the underlying transaction may give it a concomitant interest in the expression itself.<sup>276</sup> For this reason, laws restricting commercial speech, unlike laws burdening other forms of protected expression, need only be tailored in a reasonable manner to serve a substantial state interest to survive First Amendment scrutiny.<sup>277</sup> As the Supreme Court noted in *Fox*, almost all of the restrictions disallowed under the fourth prong of *Central Hudson* have been substantially excessive, disregarding "far less restrictive and more precise means."<sup>278</sup> FDA should be able to make a compelling argument that the regulation meets the "reasonable fit" test and is not overly broad, which was the problem in *WLF*. The Agency would argue that speech about unapproved uses is not banned—manufacturers may disseminate enduring materials about such uses, with certain restrictions; manufacturers are merely prohibited from listing unapproved uses on the labels and labeling of drugs. As established, this directly advances a legitimate government interest. The main argument on the other side will be that a manufacturer's speech about off-label uses has been banned. Manufacturers may only disseminate other, independent parties' speech about unapproved uses. Moreover, manufacturers could argue that a simple disclaimer would be far more effective. The court notes in *WSMC* that, if FDA were merely concerned with protecting the public from being misled about whether a drug has been FDA-approved, the Agency could require disclaimers.<sup>279</sup> Disclaimers could specifically state that the uses listed on the label were unapproved and had not been subjected to FDA's drug approval process.<sup>280</sup> Moreover, FDA could provide less drastic regulations—for example, FDA could allow the discussion of unapproved uses in labeling where the use has been discussed and tested in an

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<sup>275</sup>*Cf.* *WLF I*, 13 *F.Supp.2d* 51. The *WLF* court found that the requirement of a supplemental application directly advanced the goal of getting unapproved uses on-label.

<sup>276</sup>*See* *Edenfield*, 507 U.S. at 767, discussing *Friedman*, 440 U.S. 1 and *Ohralik*, 463 U.S. at 457.

<sup>277</sup>*See id.* at 767, citations omitted.

<sup>278</sup>*Fox*, 492 U.S. at 479, quoting *Shapero*, 486 U.S. at 476.

<sup>279</sup>*See WSMC*, 69 *F.Supp.2d* at 1308.

<sup>280</sup>*Cf. id.* See also *Pearson II*, 164 *F.3d* at 657. The court held that FDA was required to consider disclaimers as an alternative to an outright ban on advertising. See *id.*



independent clinical trial, with full disclosure of the results. This type of disclaimer would rectify FDA's concern about information from manufacturers being biased. Moreover, the disclaimer would expose manufacturers to liability for "off-label" use, which would provide an incentive to ensure safety. FDA could note that the manufacturers have still missed the Agency's concerns about the incentive to get unapproved uses on-label. Without the restrictions on promoting unapproved uses in labeling, manufacturers would have no incentive to go through the FDA approval process more than once for a particular drug or device.

A court could easily come out on either side. A court could conclude that FDA's means and ends are much more reasonable than in *WLF*, *Pearson*, or *WSMC* and that FDA's policy of disallowing unapproved uses on the labeling of prescription drugs and medical devices passes constitutional muster.<sup>281</sup> Or a court could be swayed by the policy of increased consumer access to information. Finding the promotion via labeling a constitutional right, a court could encourage FDA to soften the requirements for obtaining approval of unapproved uses or to provide an incentive to manufacturers such as an increase in the patent (monopoly).

### C. Direct-to-Consumer Advertising of Off-Label Uses

In this era of increased access to information, FDA must guard against unduly restricting commercial speech, including direct-to-consumer (DTC) off-label advertising via television, radio, and print media. The speech would easily pass the threshold question of whether it is "commercial" because the commercial aspect overwhelms the non-commercial. Under the *Bolger* factors, DTC advertisements are concededly advertisements,

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<sup>281</sup>*Cf.* *Polubinski, Closing the Channels of Communication*, *supra* note 25, at 1022. "It remains likely that a court would uphold the current regulatory scheme regardless of the test it uses." *Id.* Stevens' plurality opinion in *Liquormart* explains that when a regulation intends to "protect consumers from misleading, deceptive or aggressive sales practices, or require disclosure of beneficial consumer information, [its] purpose . . . is consistent with the reasons for according constitutional protection to commercial speech and therefore justifies less than strict review. See 44 *Liquormart*, 517 U.S. at —.

clearly refer to a specific product, and are the result of an economic motivation on the part of the drug or device manufacturer.<sup>282</sup> Consequently, a court would proceed to evaluate the regulations prohibiting DTC off-label advertising under the *Central Hudson* standard.

The toughest question for a court would be whether the advertisements regarding off-label use contain language that is false or misleading. FDA's strongest argument might be that the speech is inherently misleading because of the potential for abuse, given the speaker and the audience. Unlike with the enduring materials in *WLF*, the manufacturer would be disseminating its own speech, rather than that of others. Courts have recognized that information on off-label uses is not inherently misleading when aimed at physicians,<sup>283</sup> but no court has similarly concluded that for the general public. In *Pearson*, the D.C. Circuit rejected the notion that the proposed health claims were inherently misleading merely because FDA had not approved them, thus foreclosing that argument for FDA in the realm of dietary supplements.<sup>284</sup> Moreover, the *Pearson* court found that consumers are capable of discriminating among various health claims, noting that, "It would be as if the consumers were asked to buy something while hypnotized, and therefore they are bound to be misled. We think this contention is almost frivolous."<sup>285</sup> However, the situation is not completely analogous to the dietary supplement context. Consumers are potentially less savvy with respect to prescription drugs and medical devices than with respect to dietary supplements. Even if that is the case, however, physicians can act as filters. Still, the information must not be inaccurate with respect to end-consumers. In *Liquormart*, the Supreme Court noted that "the law has developed to ensure that advertising provides consumers with accurate information about the availability of goods and services."<sup>286</sup>

To evaluate whether the speech is inherently misleading the *WSMC* court noted its considerations: (1) whether the speech is more likely to deceive than to inform the public; (2) whether there is a substantial

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<sup>282</sup>See *Bolger*, 463 U.S. at 66-67.

<sup>283</sup>See *WLF I*, 13 F.Supp.2d at —.

<sup>284</sup>See *Pearson II*, 164 F.3d at 655.

<sup>285</sup>*Id.* at 655.

<sup>286</sup>44 *Liquormart*, 517 U.S. at 496.

possibility for deception; (3) whether the type of advertising at issue is subject to abuse; and (4) whether the intended audience has the ability to evaluate the claims made.<sup>287</sup> The off-label use information is presumably truthful. Moreover, the misleading element might be reduced or removed altogether by the use of a narrower restriction.<sup>288</sup> There remains the question of whether the problem can be solved by a disclaimer. The Supreme Court in *In re R.M.J.* made clear that if the information may be presented in a way that is not deceptive, potentially misleading information may not be prohibited by the government.<sup>289</sup> At most, the commercial speech appears to be potentially misleading. Therefore, a court would need to evaluate the restrictions on off-label DTC advertising under the remaining *Central Hudson* factors.

FDA would likely point to the general goal of protecting health and safety as the substantial government interest, similar to its arguments in *WLF*, *Pearson*, and *WSMC*. A court would have to agree that such a goal meets the substantial governmental interest requirement. In *Rubin*, the Supreme Court stated that “the Government has a significant interest in protecting the health, safety, and welfare of its citizens.”<sup>290</sup> There are few, if any, more important functions performed by any regulatory agency than the function in this hypothetical—that of ensuring, when a citizen takes a prescription drug or uses a medical device, that the individual has absolute assurance that the product is safe and effective for the condition for which her physician prescribed it.<sup>291</sup> FDA would probably assert additional interests as well, such as providing encouragement for manufacturers to get off-label uses approved. FDA approval gives consumers important information to evaluate a particular drug. The court in *WLF* concluded that encouraging manufacturers to subject off-label uses to the drug approval process is a substantial governmental interest.<sup>292</sup> Congress has determined that mandatory FDA approval of all drug uses benefits the public health, and absent a showing

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<sup>287</sup>See *WSMC*, 69 *F.Supp.2d* at —, citations omitted.

<sup>288</sup>See *id.* at 1300.

<sup>289</sup>See *In re R.M.J.*, 455 *U.S.* at 203.

<sup>290</sup>*Rubin*, 514 *U.S.* at 485.

<sup>291</sup>Cf. *WLF I*, 13 *F.Supp.2d* at 69.

<sup>292</sup>See *WLF I*, 13 *F.Supp.2d* at 71 and *WLF II*, 56 *F.Supp.2d* at 85.

of unsupportable paternalism or some other essential flaw, a court will likely accept Congress' judgment on the matter.<sup>293</sup> Consequently, a court would likely conclude that encouraging FDA approval is a legitimate goal. FDA might also assert an interest in assuring that consumers receive accurate and unbiased information in order to prevent consumer fraud. As the Supreme Court noted in *Edenfield*, the government has a substantial interest in ensuring the accuracy of commercial information in the marketplace.<sup>294</sup> Moreover, the court in *Pearson* noted that the "government's interest in preventing consumer fraud/confusion may well take on added importance in the context of a product, such as dietary supplements, that can affect the public's health."<sup>295</sup> This is a different inquiry than in *WLF*, where the court focused on the physician's ability to evaluate effectively off-label information in the form of enduring materials or CME seminars,<sup>296</sup> and determined that ensuring accurate information was *not* a legitimate interest. Thus, the government would probably succeed in its argument that limiting consumer fraud by ensuring accurate information is a legitimate substantial interest.

Having satisfied the second factor, the prohibition on off-label DTC advertisements will be evaluated under the third *Central Hudson* factor: does the regulation directly advance the governmental interests asserted?<sup>297</sup> FDA will carry the burden of justifying its restriction by demonstrating that the harms it recites are real and that its restriction will in fact alleviate them to a material degree.<sup>298</sup> FDA will need to show that the prohibition on off-label DTC advertisements will avert the following harms: the deception of the public that FDA has approved the discussed uses and the absence of an incentive to get off-label uses on-label. A court is likely to find that the restriction on off-label DTC advertisements does not directly advance the government's interest in preventing the deception of the public because disclaimers, which would not

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<sup>293</sup>Cf. *WLF II*, 56 F.Supp.2d at 86.

<sup>294</sup>See *Edenfield*, 507 U.S. at —.

<sup>295</sup>*Pearson II*, 164 F.3d at 656.

<sup>296</sup>See *WLF I*, 13 F.Supp.2d 51 & *WLF II*, 36 F.Supp.2d 16. "The government, however benign its motivations, simply cannot justify a restriction of truthful nonmisleading speech on the paternalistic assumption that such restriction is necessary to protect the listener from ignorantly or inadvertently misusing the information." 13 F.Supp.2d at 69-70.

<sup>297</sup>See *Central Hudson*, 447 U.S. at 566.

<sup>298</sup>See *Edenfield*, 507 U.S. at 770-771.

suppress speech, could more easily accomplish FDA's goal. Any potential deception of the public of this kind can be dealt with through a disclaimer, much as was suggested in *WLF* and *Pearson*. A court would probably find that the prohibition does directly advance the goal of FDA approval, however, relying on the *WLF* court's discussion regarding the supplemental application. Thus, the regulation directly advances one of the government's substantial interests.

Finally, a court will examine the fit between the government's ends and the means chosen to accomplish those ends. Restrictions designed to prevent deceptive advertising must be narrowly drawn and no more extensive than necessary to further substantial interests.<sup>299</sup> In *WLF*, the court found that the supplemental application requirement was not sufficiently narrowly tailored to achieve the legitimate goal of encouraging manufacturers to get off-label uses approved.<sup>300</sup> However, the *WLF* court noted that one of the factors in making its decision that the regulation was overly broad was that manufacturers are still much more limited in their promotion of off-label uses and that, therefore, FDA should not engage in "constitutional blackmail."<sup>301</sup> If courts take away all impediments to off-label promotion, FDA may have no tool to use to encourage manufacturers to get new uses approved. Therefore, a court might be willing to find the means/end fit reasonable with respect to the goal of getting off-label uses on-label. Moreover, the policy in favor of increased disclosure in product labeling may not similarly motivate a court with regard to DTC advertisements. DTC advertisements, particularly broadcast ones, do not provide a forum for full disclosure. Perhaps FDA might be able to argue that even in an era favoring increased consumer access to information, short-form ads are not the method with which to do it.

#### D. Internet and Off-label Uses

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<sup>299</sup>See *In re R.M.J.*, 455 U.S. at 203; *Fox*, 492 U.S. at 477.

<sup>300</sup>See *WLF II*, 56 F.Supp.2d at 87.

<sup>301</sup>See *id.*

## 1. Background

As noted, FDA strives to assure the safety and integrity of food, drugs, and cosmetics. To that end, the law has continually developed to respond to new fraudulent and dangerous medical claims. The Internet provides unprecedented opportunities to exchange information—for medical device and pharmaceutical companies as well as consumers and medical practitioners.<sup>302</sup> Consequently, FDA's intention to develop a regulatory scheme for Internet drug promotion was unsurprising.<sup>303</sup> Uncontrolled drug promotion on the Internet is a relatively recent problem.<sup>304</sup> Nevertheless, surveys indicate that disease information is already the most sought-out category of information on the Internet, and market researchers predict that the Internet will become the single greatest source of health care information within the next five years.<sup>305</sup>

One of the first issues for FDA will be to determine whether promotion on the Internet falls under "labeling" or "advertising." In 1996, the Director of CDRH's Promotion and Advertising Policy Staff noted that device information on the Internet likely constituted labeling. In his view, materials on the Internet are not "any different from promotional literature sent directly to consumers."<sup>306</sup> One commentator agrees, arguing that Internet materials should be considered labeling rather than advertising because written mate-

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<sup>302</sup>See Moberg, *Surfing the Net*, *supra* note 208, at 213.

<sup>303</sup>See Leah Brannon, *Regulating Drug Promotion on the Internet*, 54 *FOOD & DRUG L.J.* 599, 599 (1999), citing *F-D-C- REP.*, *Internet Advertising; Promotion of FDA-Regulated Medical Products on the Internet*, Notice of Public Meeting, 61 *Fed. Reg.* 48,707 (Dept. 16, 1996). A panelist at a 1996 FDA Conference of Drug Promotion on the Internet stated, "There is some frank quackery going on out there." *Id.*

<sup>304</sup>The Internet is a child of the cold war. In the 1960s, Paul Baran of the Rand Corporation, a military think tank, conceived a "fishnet" information infrastructure that could survive a nuclear attack. See Opderbeck, *How Should FDA Regulate Prescription Drug Promotion*, *supra* note 202, at 47-48. Building on that idea, the Department of Defense's Advanced Research Project Association created ARPANET, a small network that linked supercomputers located at several universities in the United States in 1969. See *id.* The commercial version, TELENET, was opened in 1974, making fast e-mail communication available to nonacademics. In 1990, ARPANET was decommissioned, leaving only the networks connected by a data transfer protocol called "TCP/IP." The Internet had a momentous year in 1991. Initially, the principal backbone of the Internet was a network maintained by the National Science Foundation called NSFNET. Although it at first banned any commercial traffic, that ban was lifted in 1991. See *id.* at 48.

<sup>305</sup>See Brannon, *Regulating Drug Promotion*, *supra* note 304, at 602.

<sup>306</sup>See *Device Information on the Internet Likely Constitutes Labeling*, M-D-D-I REP. ("The Gray Sheet"), July 15, 1996 at I and W, 5-6. See also *FDA Must Address Internet Advertising*, Former Agency Commissioner Hayes Suggests, F-D-C REP. ("The Pink Sheet"), Oct. 23, 1995.

rials on the Internet can be far more expansive than typical advertisements in journals and newspapers.<sup>307</sup> However, CDRH has taken the position that product claims on-line, other than those on manufacturers' homepages, are advertising and will be so regulated.<sup>308</sup> Other commentators have argued that, because the Internet depends on "telephone communications systems," FDA has little choice but to classify all information broadcast across the Internet as "advertisements."<sup>309</sup> If this is the case, FDA will have authority to regulate only promotions of prescription drugs and restricted medical devices, leaving over-the-counter drug promotions to the FTC.<sup>310</sup>

The Internet presents novel issues that FDA's regulations and guidance originally did not contemplate. FDA has not issued any formal guidance that addresses specifically the novel promotional issues presented by increasing use of the Internet. While FDA is developing a formal policy with respect to promotion on the Internet, companies have been advised to "ask themselves whether the information they seek to post would be permissible on 'hard copy.'"<sup>311</sup> Currently, FDA initiates enforcement actions against specific Internet promotions it considers false and misleading. Usually, FDA targets websites promoting products without clearance, off-label uses, or otherwise employing misleading or unsupported claims. For example, FDA sent a warning letter to a manufacturer of a uterine balloon therapy system promoted on the manufacturer's homepage for use in the treatment of menorrhagia.<sup>312</sup> FDA had not cleared the device for menorrhagia; consequently, the Agency declared that such promotion rendered the device adulterated under the FD&C Act.<sup>313</sup> FDA has reacted similarly to links on manufacturer homepages to sites discussing off-label use. FDA has issued a warning letter to a manufacturer of a transurethral injection needle system and injec-

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<sup>307</sup>See Marc J. Scheineson, *Legal Overview of Likely FDA Regulation of Internet Promotion*, 51 *FOOD & DRUG L.J.* 697 (1996).

<sup>308</sup>See Moberg, *Surfing the Net*, *supra* note 208, at 219.

<sup>309</sup>Brannon, *Regulating Drug Promotion*, *supra* note 304, at 603. The definition for advertising includes "'telephone communications systems.'" 21 C.F.R. § 201(1)(1)(1996).

<sup>310</sup>See 21 U.S.C. § 502(n).

<sup>311</sup>Moberg, *Surfing the Net*, *supra* note 208, at 219, citations omitted.

<sup>312</sup>See, *Director, Office of Compliance, CDRH to Gynecare, Inc. (Feb. 5, 1997)*.

<sup>313</sup>See *id.*

tion/aspiration needle device concerning the links provided on its website.<sup>314</sup> FDA stated that the material presented on the website modified the manufacturer's intended use for the product and resulted in the misbranding and adulteration of both devices.<sup>315</sup> FDA specifically pointed out a link on the website to an article which included a statement that "the delivery of adenoviral vectors directly to the prostate provided the 'best route to treat local prostate cancer by viral-based gene therapy.'" <sup>316</sup> Although there was no explicit reference to the manufacturer's products in the article, FDA concluded that the implication created by the link along with a picture of the device after the article was sufficient to result in the misbranding of the devices.<sup>317</sup> Consumer groups, medical associations, and even some drug producers have called on FDA to develop a comprehensive regulatory approach.<sup>318</sup>

## 2. *First Amendment Analysis*

Aside from the practical difficulties of FDA's regulating promotion of off-label uses on the Internet, the Agency may face constitutional impediments as well.<sup>319</sup> Because many cases have held that more information is preferable to less, FDA may not be able to stifle commercial speech about unapproved uses. Whether FDA may constitutionally restrict off-label promotion on the Internet will turn on an analysis of what type of speech is at issue and an evaluation of the restriction under the appropriate standard. Much of the analysis will turn on the speaker's identity. FDA may not restrict the discussion of unapproved uses by non-manufacturers, nor does the Agency restrict the prescription of drugs and medical devices for unapproved uses; moreover, the Agency may not prevent a manufacturer from disseminating enduring materials that discuss off-label use to certain groups. If FDA were to prevent the discussion of off-label uses by non-

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<sup>314</sup>See *Basile, Medical Device*, *supra* note 198, at 531, discussing *Letter to Gynecare*.

<sup>315</sup>See *id.*

<sup>316</sup>See *id.*

<sup>317</sup>See *id.*

<sup>318</sup>See *Brannon, Regulating Drug Promotion*, *supra* note 304, at 602.

<sup>319</sup>For a good discussion of the practical difficulties of regulating promotion on the Internet, see *Brannon, Regulating Drug Promotion*, *supra* note 304, at ---.



manufacturers, an analysis would likely determine that the speech deserved full First Amendment protection. Consequently, FDA will need to construct its regulations to avoid an overly broad suppression of speech. Given the warning letters FDA has sent to manufacturers, it appears that the Agency plans to prohibit not only the discussion by the manufacturer of off-label uses, but also the reference to sites which discuss such uses. This paper analyzes such restrictions under the First Amendment.

As the discussion above indicates, the speech is a hybrid of “labeling” and “advertising,” with both commercial and non-commercial aspects. Much as the Supreme Court did in *Bolger* and *Fox*, a court would need to evaluate the speech and would likely conclude that speech directly on a manufacturer’s homepage should be categorized as commercial speech. The economic motive of the speaker is clear and there will be at least a tacit, if not explicit, reference to a specific product. These two factors would probably outweigh the argument that the speech is not concededly an advertisement, but perhaps a scientific discussion of the merits of an approved drug for unapproved uses. Once under the commercial speech designation, a court would consider the four factors of *Central Hudson*. The analysis of the links would be analogous to that of the enduring materials in *WLF*, with the exception of the recipients’ identity. A court would likely conclude that the manufacturers endeavor through the links to increase the sales volume of their drugs, and that the speech is commercial in nature.<sup>320</sup> A strong argument can be made, nonetheless, that the speech is “pure” and thus entitled to full First Amendment protection: the linked sites are not necessarily advertisements, do not necessarily mention the product name, and consumers who invoke their right to receive the information may have no economic motivation at all.<sup>321</sup>

Is the speech targeted by the prohibition constitutionally protected?<sup>322</sup> It is unlikely that FDA can make a viable argument that the speech is not constitutionally protected because it is misleading. Under *Central*

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<sup>320</sup>Cf. *WLF I*, 13 *F.Supp.2d* at 64.

<sup>321</sup>For a similar argument in the context of enduring materials, see Murphy, “‘It’s Time to Make a Good Agency Better,’” *supra* note 9, at 621.

<sup>322</sup>See *Central Hudson*, 447 *U.S.* at 566.

*Hudson*, “for commercial speech to come within [First Amendment protection], it must at least concern lawful activity and not be misleading.”<sup>323</sup> The speech about off-label uses concerns lawful activity because FDA does not prohibit the prescription or use of a drug or device for non-approved purposes. Moreover, FDA has consistently failed to demonstrate that speech about off-label use is inherently misleading. In evaluating whether the speech is misleading, a court will consider whether the speech is “more likely to deceive the public than to inform it.”<sup>324</sup> As for the information on a manufacturer’s homepage, the fact that the manufacturer is the speaker might cause confusion that the use is FDA-approved, but this can easily be resolved through disclaimers, as in *Pearson*. With respect to links to sites that discuss off-label use, a court would likely rely on the analysis in *WLF* to conclude that the speech is not likely to deceive the public. Only when a manufacturer initiates the exchange of information through the use of a link does FDA choose to label the speech false or inherently misleading. The Supreme Court has recently addressed this situation, noting, “Even under the degree of scrutiny that we have applied in commercial speech cases, decisions that select among speakers conveying virtually identical messages are in serious tension with the principles undergirding the First Amendment.”<sup>325</sup> Consequently, a court should conclude the speech provided via the links at issue is not inherently misleading. The next questions a court would consider in evaluating the “inherently misleading” nature of the speech, as advanced by FDA, are whether there are substantial “possibilities for deception”<sup>326</sup> and “whether experience has shown that such advertising is subject to abuse.”<sup>327</sup> Analysis of the discussion of unapproved uses on the manufacturer’s website would be similar to that of listing unapproved uses in labeling (primarily because FDA would currently regulate such information as “labeling”). With respect to links to sites discussing off-label use, it is quite analogous to *WLF* and the dissemination

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<sup>323</sup>*Id.*

<sup>324</sup>*Id.* at 563.

<sup>325</sup>*Greater New Orleans Broad. Assoc. v. U.S., --- U.S. ---, 119 S.Ct. 1923, 1935 (1999).*

<sup>326</sup>*Friedman*, 440 U.S. at 13.

<sup>327</sup>*In re R.M.J.*, 455 U.S. at 203.

of enduring materials.<sup>328</sup> While FDA might be able to require that the linked pages meet the same requirements as the enduring materials under FDAMA, the Agency could likely not ban listing links as inherently misleading. Finally, a court would consider whether the intended audience has the ability to evaluate the claims made.<sup>329</sup> FDA's strongest argument will be similar to that under DTC advertising of off-label uses. Although most information on the Internet is written for medical practitioners, everyone has access to the information.<sup>330</sup> Nevertheless, broad access alone should not cause the speech to be inherently misleading and outside First Amendment protection altogether. Thus, the court will proceed with the remainder of the *Central Hudson* factors.

Second, a court will consider whether the government asserts a substantial interest in prohibiting off-label discussion and links on manufacturer homepages.<sup>331</sup> FDA can point to the general goal of protecting the public health and safety without challenge.<sup>332</sup> More specific goals FDA might assert include those asserted previously with respect to putting unapproved uses in labeling and disseminating enduring materials discussing off-label uses. In *WLF*, FDA asserted an interest in the accuracy of information and the incentive to get unapproved uses approved by the Agency. In *Pearson*, FDA advanced an interest in preventing the confusion of consumers. The *WLF* and the *Pearson* courts rejected the interests in accurate information and prevention of confusion as overly paternalistic. As in the labeling context, however, a court could easily determine that ensuring accurate information is a legitimate goal, especially in the context of the Internet, where information and its source can be questionable. A court would likely conclude much as in *Pearson* and the DTC advertising context that the prevention of consumer confusion is not a legitimate goal. A disclaimer would resolve FDA's concern. The interest in the approval of unapproved uses continues to be the most persuasive, and a court would likely agree with the *WLF* decision that encouraging FDA approval

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<sup>328</sup>See *WLF I*, 13 *F.Supp.2d* 51 and *WLF III*, 56 *F.Supp.2d* 81.

<sup>329</sup>See *In re R.M.J.*, 455 U.S. at 203.

<sup>330</sup>See *Brannon, Regulating Drug Promotion*, *supra* note 304, at —.

<sup>331</sup>See *Central Hudson*, 447 U.S. at —.

<sup>332</sup>See, e.g., *Rubin*, 514 U.S. at 485, and *WSMC*, 69 *F.Supp.2d* at 1301.

is a legitimate goal.

Under the third *Central Hudson* factor, a court will consider whether the two substantial governmental interests are directly advanced by the prohibition of off-label discussion or links to sites with off-label discussion on manufacturers' homepages. The prohibition does not advance the goal of ensuring accurate and unbiased information, because more disclosures rather than less would best serve this goal. Much as in the labeling and DTC advertising contexts, however, the goal of encouraging formal approval of unapproved uses does seem advanced by the broad prohibition. Nevertheless, the prohibition on providing informative links fails the ends and means test because it is not "reasonable" and results in a broad suppression of speech. Consequently, FDA can probably continue to suppress manufacturer's own speech about off-label uses on Internet homepages, but not the provision of materials similar to the enduring materials in *WLF*.

## CONCLUSION

In conclusion, FDA may continue to suppress some forms of discussion about off-label use, primarily where there is little opportunity to evaluate the information and no independent research is included (such as in short Direct-to-Consumer advertisements and possibly on homepages). As the ability to access information continues to grow, however, FDA will probably be forced to allow the increased promotion of unapproved uses.