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## OFF-LABEL “PROMOTION” MAY NOT BE MERELY COMMERCIAL SPEECH.

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*Most attorneys (whether in practice or academia) assume that pharmaceutical companies’ discussion and dissemination of information regarding “off-label” uses of prescription drugs (i.e., uses that have not been specifically approved by the Food and Drug Administration (FDA)) are inherently commercial in nature. Two aspects of the speech, however, suggest that it does not cleanly fall into the category of “commercial speech” for purposes of First Amendment analysis. First, most prescribers are not, in fact, purchasing drugs for their patients, and so conversations between pharmaceutical company representatives and prescribers are not directly linked to a commercial transaction the same way they are with an advertisement or sales pitch to an end consumer. Second, prescribers are “learned intermediaries,” charged by profession and law to research and weigh the range of potential risks and benefits of each product they prescribe for their patients, whether it is prescribed for an FDA-approved use or an off-label use. As a result, scientific and medical information is “inextricably linked” to any speech that would be considered merely commercial. Prior attempts to restrict speech that included both financially driven and noncommercial components have received exceptionally rigorous scrutiny when reviewed by the Supreme Court. This Article suggests that the current restrictions on some pharmaceutical company speech may be given what I shall call “enhanced intermediate” (or even strict) scrutiny, rather than the usual intermediate scrutiny given to restrictions of merely commercial speech, because of the unique professional and legal role played by prescribers.*

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#### INTRODUCTION

In a recent New York Times article, the reporters criticized a biotechnology company’s current marketing strategy of “persuading eye doctors to start using its new more expensive drug instead of a popular cheaper version that the company already sold.”<sup>1</sup> More specifically, instead of advising prescribers to use Genentech’s cancer drug, Avastin, to treat their wet macular degeneration patients (at a cost of around fifty dollars per dose), the company’s sales representatives were encouraging ophthalmologists to treat this common eye disease in the elderly with Lucentis, “a nearly equivalent drug that cost \$2,000 a dose.”<sup>2</sup>

What was particularly interesting about this article was that it implicitly called for Genentech to either (1) underpromote Lucentis, a newer and likely more profitable product (potentially running afoul of the for-profit corporation’s fiduciary duty to its shareholders); or (2) promote Avastin for a use unapproved by the FDA (and risk criminal liability and False Claims Act exposure for “off-label” promotion<sup>3</sup>). Avastin, despite being the standard of care for wet macular

1. Katie Thomas & Rachel Abrams, *Paid to Promote Eye Drug, and Prescribing It Widely*, N.Y. TIMES (Dec. 7, 2014), <http://www.nytimes.com/2014/12/08/business/paid-to-promote-eye-drug-and-prescribing-it-widely-.html>.

2. *Id.*

3. Genentech settled False Claims Act allegations of off-label promotion related to another cancer drug, Rituxan, for \$20 million in November 2011. Ron Leuty, *Genentech Settles Rituxan Whistleblower Suit for \$20M*, S.F. BUS. TIMES (Dec. 2, 2011, 10:37 AM), <http://www.bizjournals.com/sanfrancisco/blog/biotech/2011/12/genentech-roche-rituxan-whistleblower.html?page=all>.

degeneration,<sup>4</sup> is FDA approved only for treating a number of different types of cancer.<sup>5</sup> Lucentis, by contrast, is FDA approved for neovascular (wet) age-related macular degeneration, macular edema following retinal vein occlusion, diabetic macular edema, and diabetic retinopathy in patients with diabetic macular edema.<sup>6</sup>

Off-label prescription and use of prescription drugs is legal, and even the FDA concedes that it can be beneficial to patients or the standard of care (as in the case of Avastin).<sup>7</sup> Despite the myriad multimillion and billion dollar settlements between industry and the federal government, the legality of off-label promotion by biotechnology and pharmaceutical companies remains unclear.<sup>8</sup> The practice is often broadly painted as a threat to public health with the potential to increase prescription and use of unnecessary, unsafe, or more expensive drugs.<sup>9</sup> These public health concerns tend to be laid at the feet of pharmaceutical manufacturers despite the critical role that prescribers play.<sup>10</sup> Indeed, prescribers

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4. CATT Research Grp., *Ranibizumab and Bevacizumab for Neovascular Age-Related Macular Degeneration*, 364 NEW ENG. J. MED. 1897, 1898 (2011) (“Bevacizumab [Avastin] is the most commonly used drug in the United States for the treatment of neovascular AMD, despite the absence of large-scale clinical-trial data supporting its use.”); *see also* Thomas & Abrams, *supra* note 1 (“Avastin is still the most popular choice of doctors: About half of patients who were treated for wet macular degeneration received Avastin, with Lucentis and Eylea sharing the rest of the market.”).

5. GENETECH, INC., AVASTIN: HIGHLIGHTS OF PRESCRIBING INFORMATION 1 (2015), [http://www.gene.com/download/pdf/avastin\\_prescribing.pdf](http://www.gene.com/download/pdf/avastin_prescribing.pdf) (describing the different forms of cancer that Avastin is approved to treat).

6. *See* GENETECH, INC., LUCENTIS: HIGHLIGHTS OF PRESCRIBING INFORMATION 1 (2015), [http://www.gene.com/download/pdf/lucentis\\_prescribing.pdf](http://www.gene.com/download/pdf/lucentis_prescribing.pdf) (explaining the various treatment usages for Lucentis).

7. *Guidance for Industry: Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices*, U.S. FOOD & DRUG ADMIN. (2009), <http://www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm> [hereinafter FDA, *Good Reprint Practices*] (“Once a drug or medical device has been approved or cleared by FDA, generally, healthcare professionals may lawfully use or prescribe that product for uses or treatment regimens that are not included in the product’s approved labeling (or, in the case of a medical device cleared under the 510(k) process, in the product’s statement of intended uses). These off-label uses or treatment regimens may be important and may even constitute a medically recognized standard of care.”).

8. *See generally* Stephanie M. Greene & Lars Noah, *Off-Label Drug Promotion and the First Amendment*, 162 U. PA. L. REV. ONLINE 239 (2014). *See* Complaint at 7, *Amarin Pharma, Inc. v. U.S. Food & Drug Admin.*, No. 15 CV 3588, 2015 WL 2128126 (S.D.N.Y. filed May 7, 2015) (alleging that the FDA’s regulation of off-label promotion is unconstitutional under the First Amendment); *see also* *Amarin Pharma, Inc. v. U.S. Food & Drug Admin.*, No. 15 CIV. 3588 (PAE), 2015 WL 4720039, at \*1 (S.D.N.Y. Aug. 7, 2015) (granting preliminary injunction because manufacturer was likely to succeed on First Amendment claim).

9. *See, e.g.*, Greene & Noah, *supra* note 8, at 241 (arguing that “pharmaceutical companies take advantage of the doctor’s right to prescribe off-label, targeting doctors in order to reach new markets for unapproved uses, and thereby avoiding the time and expense required by the FDA approval process”).

10. *See Last Week Tonight with John Oliver: Marketing to Doctors* (HBO television broadcast Feb. 8, 2015) (“Drugs aren’t like most other products because you need someone’s permission to buy them, which is why all drug ads end with the same catchy phrase: *ask your doctor*. . . . Even in its best form, hiring doctors as paid spokesmen seems like a conflict of interest. And multiple reports have

are often dismissed from the analysis as susceptible to pharmaceutical company marketing techniques and unable “to distinguish between valid and misleading information” related to prescription products.<sup>11</sup> In this attempt to simplify off-label promotion and use of prescription drugs as a problem caused primarily (if not solely) by the pharmaceutical industry, critics of off-label promotion run the very real risk of minimizing the complexity and nuance of both prescription drugs and patient care.

While the FDA attempts to ensure that all approved drugs are safe and effective for their intended uses,<sup>12</sup> both “safety” and “efficacy” are inherently relative terms in the context of prescription drugs. Prescription drugs are available only by prescription precisely because they are not “safe” enough for the public to use without professionally trained and licensed supervision.<sup>13</sup> Every drug, and indeed every use of every drug considered by the FDA, undergoes an independent risk-benefit review by the agency to determine whether the anticipated efficacy is worth the potential safety risks.<sup>14</sup> No prescription drug is safe or effective for everyone; each carries an inherent risk of unwanted adverse effects to a patient. By necessity, the FDA curates much of the relevant information used to evaluate the risk-benefit profile of a particular product. The FDA-approved labeling for any product provides a wealth of this information. The label is not, however, all-inclusive of the information on how the product has been or might be used to treat patients.

Similarly, patient care itself carries inherent risks<sup>15</sup> and is accordingly legally limited to those professionals licensed after years of education and training. Dismissing the critical role of prescribers in First Amendment analysis of off-label promotion is inconsistent with the larger legal framework, which specifically entrusts these professionals (rather than for-profit corporations) with patient care.<sup>16</sup> This dismissal runs the risk of relieving these same professionals of the

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found that many drugs’ top prescribers are also often getting money from that drug’s company, which is worrying, because *we trust doctors*.” (emphasis added)).

11. Greene & Noah, *supra* note 8, at 241–43 (citing JEROME GROOPMAN, HOW DOCTORS THINK 221 (2007)); and then citing Adriane Fugh-Berman & Shahram Ahari, *Following the Script: How Drug Reps Make Friends and Influence Doctors*, 4 PLOS MED. 621, 623–24 (2007)).

12. See 21 U.S.C.A. § 393(b)(1)(B) (West 2015) (stating that the FDA must protect the public health by providing only safe and effective drugs).

13. See *United States v. Rutherford*, 442 U.S. 544, 555 (1979) (“Few if any drugs are completely safe in the sense that they may be taken by all persons in all circumstances without risk.”).

14. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES—RECOMMENDED PRACTICES 3 (2014), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm387652.pdf> [hereinafter FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES] (“A separate balancing of risks and benefits is necessary for each intended use.”).

15. See Lisa Rosenbaum, *Being Like Mike—Fear, Trust, and the Tragic Death of Michael Davidson*, 372 NEW ENG. J. MED. 798, 799 (2015) (describing the various risks associated with patient care and stressing that “[a] mistake is not the same as a bad outcome”).

16. Thea Cohen, *The First Amendment and the Regulation of Pharmaceutical Marketing: Challenges to the Constitutionality of the FDA’s Interpretation of the Food, Drug, and Cosmetics Act*, 49 AM. CRIM. L. REV. 1945, 1967 (2012) (“We trust [prescribers] to make life or death decisions, even

legal and ethical duties they have to their patients. As part of their fiduciary duty to use independent judgment to care for their patients, these prescribers need both the information curated by the FDA and provided in the approved labeling, as well as off-label information for treating individual patients who do not neatly fit within the four corners of the drug label. Under the current federal policies, however, pharmaceutical companies and their employees risk criminal investigation, indictment, and prosecution for discussing or disseminating information about off-label uses of prescription drugs.

These policies restrict off-label speech by pharmaceutical companies based on specific content (i.e., potential uses for prescription drugs that have not been approved by the FDA), viewpoint (i.e., an off-label use may benefit a patient), and speaker (i.e., pharmaceutical company detailers are not allowed to discuss off-label uses with prescribers, but independent researchers may say the exact same thing to prescribers). In other contexts, these types of content-, speaker-, and viewpoint-based restrictions have received strict scrutiny from the Supreme Court, even when the speech would have been otherwise unprotected (i.e., “fighting words”).<sup>17</sup> While a few courts have already found that the federal government’s policies fail the intermediate scrutiny usually afforded merely commercial speech,<sup>18</sup> governmental policies that specifically target truthful statements made by pharmaceutical company representatives providing prescribers information about off-label uses of prescription drugs are likely to receive enhanced intermediate, if not strict, scrutiny.<sup>19</sup>

This Article begins in Section I with an overview of the current less-than-straightforward legal theories and FDA policies used to limit the discussion and dissemination of information on off-label uses of prescription drugs. Section II then explores the historic roles of both speaker and (the often underappreciated) listener in First Amendment analysis of whether speech restricted due to its content and viewpoint is properly considered “commercial” in nature. After these foundational sections, Section III reexamines the historic federal cases that anchor the current discussion of the constitutionality of off-label promotion of prescription drugs and identifies a number of flawed assumptions. In light of these

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absent specific government approval. We should also trust [prescribers] to be able to evaluate health-related information, whatever its source, so long as the information is not misleading or untrue.”).

17. See, e.g., *R.A.V. v. City of St. Paul*, 505 U.S. 377, 391 (1992) (applying strict scrutiny to a city ordinance prohibiting symbols or displays that insult or provoke violence “on the basis of race, color, creed, religion or gender,” including burning crosses and displaying swastikas, because it was both a content- and viewpoint-based restriction of speech).

18. See, e.g., *United States v. Caronia*, 703 F.3d 149, 167 (2d Cir. 2012); *Amarin Pharma, Inc. v. U.S. Food & Drug Admin.*, No. 15 CIV. 3588 (PAE), 2015 WL 4720039, at \*36 (S.D.N.Y. Aug. 7, 2015); *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 74 (D.D.C. 1998), *amended by* 36 F. Supp. 2d 16 (D.D.C. 1999), *appeal dismissed, judgment vacated in part sub nom. Wash. Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000).

19. Aaron S. Kesselheim & Michelle M. Mello, *Prospects for Regulation of Off-Label Drug Promotion in an Era of Expanding Commercial Speech Protection*, 92 N.C. L. REV. 1539, 1561 (2014) (“[I]t is clear that governmental restrictions on truthful statements about pharmaceuticals will be judged under an elevated level of scrutiny that is at least as stringent as the *Central Hudson* test, and perhaps higher.” (emphasis added)).

problematic assumptions, Sections IV and V argue that the unique legal, ethical, and professional roles of the prescriber-listener strongly suggest that truthful, nonmisleading communications between pharmaceutical companies and prescribers are not inherently, always, or merely commercial in nature. The Article concludes that instead of being subjected to the intermediate level of scrutiny usually reserved for restrictions on commercial speech, the government's attempts to restrict off-label speech between pharmaceutical companies and prescribers may need to survive enhanced intermediate scrutiny or the strict scrutiny usually given to content-, speaker-, and viewpoint-based restrictions on speech that is not merely commercial.

#### I. HOW DOES THE FEDERAL GOVERNMENT USE THE LAW TO BAN OFF-LABEL PROMOTION?

While FDA guidance<sup>20</sup> and Department of Justice press releases<sup>21</sup> seem to suggest that all off-label promotion of prescription drugs is illegal under federal law, the statutory and regulatory framework supporting the premise is hardly straightforward. The Food, Drug and Cosmetic Act (FDCA) and "its accompanying regulations do not expressly prohibit or criminalize off-label promotion."<sup>22</sup> Instead, the ban on off-label promotion is based largely on agency regulations interpreting the FDCA provisions pertaining to "labeling," requirements for "new drugs," and "misbranding."<sup>23</sup> Each of these is explained in turn below.

##### A. Defining "Off-Label Promotion"

The regularity with which the term "off-label promotion" is used by the government, industry, media, and the academy alike suggests a common understanding, indeed, an actual definition. The term, however, has never been defined by statute or regulation. It is, instead, an umbrella term used to characterize a wide array of both conduct and speech related to the marketing and sales of prescription drugs.

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20. E.g., Press Release, Office of Pub. Affairs, U.S. Dep't of Justice, *Abbott Labs to Pay \$1.5 Billion to Resolve Criminal & Civil Investigations of Off-label Promotion of Depakote* (May 7, 2012), <http://www.justice.gov/opa/pr/abbott-labs-pay-15-billion-resolve-criminal-civil-investigations-label-promotion-depakote> ("Under the Food, Drug and Cosmetic Act (FDCA), a company in its application to the FDA must specify each intended use of a drug. A company's promotional activities must be limited to only the intended uses that FDA approved.").

21. E.g., FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 3.

22. *Caronia*, 703 F.3d at 160.

23. PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, *FOOD AND DRUG LAW: CASES AND MATERIALS* 926 (4th ed. 2014).

### 1. What Is This “Label”?

Labels and labeling define the scope of the legal and regulatory framework for prescription drugs.<sup>24</sup> The various statutory and regulatory definitions of “label,”<sup>25</sup> “labeling”<sup>26</sup> and “advertising”<sup>27</sup> include exclusively written, auditory, or visual (and thus, inherently fixed) media—not real-time or in-person conversations.<sup>28</sup>

For each prescription drug the FDA reviews, it requires the sponsoring pharmaceutical company to submit proposed labeling as part of the new drug application.<sup>29</sup> Unlike the labels for products available over the counter, prescription drug labeling is not intended to provide laypeople with information on the drug, but rather “practitioners licensed by law to administer the drug”<sup>30</sup> with information on the “indications, effects, dosages, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side

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24. Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the FDA, 37 Fed. Reg. 16503, 16503 (proposed Aug. 15, 1972) (codified at 21 C.F.R. pt. 130) (emphasis added). “The major objective of the drug provisions of the [FDCA] is to assure that drugs will be safe and effective for use under the conditions of use prescribed, recommended, or suggested in the labeling thereof.” *Id.*

25. As defined by the FDCA, a “label” is generally “a display of written, printed, or graphic matter upon the immediate container of any article.” 21 U.S.C.A. § 321(k) (West 2015). The FDA further defined a label to be “any display of written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.” 21 C.F.R. § 1.3(b) (2015).

26. “Labeling” includes “all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article,” 21 U.S.C.A. § 453(s), as well as “all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that drug.” *Id.* § 352(n); *see also* 21 C.F.R. § 1.3(a) (“Labeling includes all written, printed, or graphic matter accompanying an article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.”). “[T]he phrase ‘accompanying such article’ is not restricted to labels that are on or in the article on package that is transported.” *Kordel v. United States*, 335 U.S. 345, 349 (1948). Instead, it may be sufficient for drugs and literature to have “a common origin and a common destination.” *Id.* at 348. Literature has been considered “accompanying” drugs and, thus “labeling,” despite the fact that they were not sent together through interstate commerce. *Id.* at 347–49.

27. As delineated in the Code of Federal Regulations, “advertising” includes “advertisements in published journals, magazines, other periodicals, and newspapers, and advertisements broadcast through media such as radio, television, and telephone communication systems,” along with

[b]rochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, motion picture films, film strips, lantern slides, sound recordings, exhibits, literature, and reprints and similar pieces of printed, audio, or visual matter descriptive of a drug and references published (for example, the “Physicians Desk Reference”) for use by medical practitioners, pharmacists, or nurses containing drug information supplied by the manufacturer, packer, or distributor of the drug and which are disseminated by or on behalf of its manufacturer.

21 C.F.R. § 202.1(l)–(2).

28. The FDA has no direct statutory or regulatory authority over oral statements made by pharmaceutical company representatives because they are neither labeling nor advertising. *HUTT ET AL.*, *supra* note 23, at 912.

29. 21 U.S.C.A. § 355(b)(1)(F).

30. 21 C.F.R. § 201.100(a)(iii).

effects, and precautions” informed by the clinical trials supporting the new drug application.<sup>31</sup>

The new drug approval process is an iterative, multifaceted negotiation that includes a risk-benefit assessment, “regulatory decisionmaking, and the communication of the benefits and risks of new drugs.”<sup>32</sup> The FDCA does not identify the number or type of trials necessary for approval of a prescription drug, but rather delegates the responsibility of determining what level of scientific or medical evidence should suffice to demonstrate the “safety and efficacy” of a drug to the FDA.<sup>33</sup> The FDCA requires “adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof,”<sup>34</sup> and “substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof.”<sup>35</sup>

Most drug companies meet with the FDA early in the drug development process to negotiate the structure of the Phase 3 clinical trials, including selection of relevant measurements and endpoints, trial duration, and inclusion and exclusion criteria for the trials.<sup>36</sup> While the FDA has historically required pharmaceutical companies to conduct two large-scale, prospective, placebo-controlled, double-blind trials to demonstrate the safety and efficacy required by the FDCA, the agency has been responding to pressure from patient groups and industry to approve new drugs more quickly, especially those designed for rarer and more severe diseases and conditions.<sup>37</sup> The FDA has discretion to approve drugs based on alternative forms of evidence.<sup>38</sup>

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31. *Id.* § 201.100(c)(1).

32. 21 U.S.C.A. § 355(d). Indeed, a separate risk-benefit assessment is conducted not only for each drug, but for each use for each drug. FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 2–3.

33. *See* 21 U.S.C.A. § 355(b)(5)(B)–(C).

34. 21 U.S.C.A. § 355(d).

35. *Id.* (defining “substantial evidence” as “evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling”).

36. *Amarin Pharma, Inc. v. U.S. Food & Drug Admin.*, No. 15 CIV. 3588 (PAE), 2015 WL 4720039, at \*9 (S.D.N.Y. Aug. 7, 2015) (describing the FDA’s “special protocol assessment” (SPA) program where a manufacturer may enter into a written agreement with the FDA describing the design and size parameters for clinical trials of a new drug, and the conditions under which the FDA would approve the drug).

37. *See* JONATHAN D. MORENO, *THE BODY POLITIC: THE BATTLE OVER SCIENCE IN AMERICA* 25 (2011) (“It is now common to speak of ‘disease communities,’ a twentieth-century form of affiliation and self- and mutual identification. Those advocating on behalf of research funding for diseases that are too uncommon to have much political clout on their own have organized into rare disease coalitions.”); Amy Dockser Marcus, *A Patients’ Group Scores a Win in Muscular Dystrophy Drug Research*, *WALL ST. J.* (Aug. 4, 2014), <http://www.wsj.com/articles/a-patients-group-scores-a-win-in-muscular-dystrophy-drug-research-1407194541> (“When it comes to developing new drugs, pharmaceu-

A drug is not considered approved until the FDA approves its label language.<sup>39</sup> The pharmaceutical company and the FDA negotiate the specific wording of the lengthy product information to be included with all sales of a drug to pharmacists and discussions of the product with prescribers.<sup>40</sup> Once approved by the FDA, it is this particular labeling, also known as the “prescribing information,”<sup>41</sup> that is used to determine whether a particular use is considered an “on-label” or “off-label” use of a drug.<sup>42</sup> This product information, generally understood to be the “label” of a drug, includes a tremendous amount of information about the drug, but reflects only the information considered relevant by the FDA.<sup>43</sup> Perhaps not surprisingly, pharmaceutical companies and FDA offi-

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tical companies and federal agencies have always called the shots. Now patients and their families want a turn. Parent Project Muscular Dystrophy, an advocacy group founded by family members frustrated by a lack of research on Duchenne muscular dystrophy, initiated and wrote a draft guidance for pharmaceutical companies trying to develop drugs to treat the fatal condition. Guidances are issued by the [FDA] and set out the latest thinking on designing trials and which standards must be met by companies to get a new drug approved. The FDA typically initiates the creation of guidances. But with so many diseases, the agency can’t cover them all. The Duchenne draft guidance, written by a committee of over 80 parents, scientists, drug company executives and clinicians, was submitted to the FDA in late June with the hope all or most of it would be formally adopted by the agency.”).

38. 21 U.S.C.A. § 355(d) (“If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.”).

39. See Transcript of Advisory Committee Meeting on Psychopharmacological Drugs at 10, U.S. Dep’t of Health & Human Servs., U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research (2000), <http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3690t1a.pdf> (statement of Thomas Laughren, Team Leader for Psychopharmacology, U.S. Food & Drug Admin.) (explaining that in order for the FDA to approve a new drug, the drug’s labeling must be found to be acceptable).

40. See *id.* at 11 (statement of Thomas Laughren, Team Leader for Psychopharmacology, U.S. Food & Drug Admin.) (“[A New Drug Application] must have labeling proposed to be used for such a drug, and that would include language describing the indication. The Secretary may refuse to approve an application if, based on a fair evaluation of all material facts, such labeling is false or misleading in any particular. In this context, we would argue that a poorly defined indication is potentially misleading since, in that situation, it would not be possible to inform prescribers about how to use the drug if we can’t define what the indication is.”).

41. See *Drug Advertising: A Glossary of Terms*, U.S. Food & Drug Admin., [http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072025.htm#prescribing\\_information](http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072025.htm#prescribing_information) (last visited Nov. 1, 2015) (“Prescribing information is also called product information, product labeling, or the package insert (‘the PI’). It is generally drafted by the drug company and approved by the FDA.”).

42. The FDA tends to use the terms “unapproved new use,” “unapproved use,” and “off-label use” interchangeably “to refer to a use of an approved or cleared medical product that is not included in the product’s approved labeling.” FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 1 n.4.

43. The FDA’s policies on how labeling language ought to be generated and curated has evolved over time. As one example, psychotropic drug labeling underwent a significant shift in the very early twenty-first century from broad language describing the symptoms prescribers were treating (e.g., “short-term relief of the symptoms of anxiety” or “management of the manifestations of psychotic disorders”) to much more specific language describing the specific diagnoses of the patients studied in the clinical trials (e.g., “treatment of obsessive-compulsive disorder” or “treatment of schizophrenia”). Transcript of Mar. 9, 2000 Meeting at 13–18, U.S. Food & Drug Admin., Ctr. for Drug Evalua-

cials often disagree about what wording best reflects the data generated by the clinical trials. The label remains a negotiated document between the company and the FDA throughout a drug's lifespan and may be updated over time to reflect new clinical data, potentially new indications, newly observed adverse effects,<sup>44</sup> or new statutory, regulatory, or policy requirements. It is this specific, negotiated wording on the prescribing information that draws the line between "on-label" and "off-label" speech.<sup>45</sup>

## 2. What Is "Promotion"?

Rather than describing a singular type of communication, "promotion" of a prescription drug can take a number of different modes and forms of communication across a continuum of legality.<sup>46</sup> Table 1 discusses speech and conduct that has been characterized as promotion by the U.S. Department of Justice and the FDA.

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tion & Research, Psychopharmacologic Drug Advisory Comm., <http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3690t1a.pdf>; see also Transcript of July 19, 2000 Meeting at 157–58, U.S. Food & Drug Admin., Ctr. for Drug Evaluation & Research, Psychopharmacologic Drug Advisory Comm., <http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3619t1b.pdf>. In response to a question of whether the drug Mellaril was currently indicated for the broader indication of "psychosis" or narrower indication of "schizophrenia," FDA presenter Dr. Dubitsky described the agency's ongoing work to "make labeling more clear as far as the specific indications, and to link those to the indications that were actually studied in the pivotal trials that led to the approval." *Id.* at 158. Dr. Laughren confirmed that this shift in labeling language was

really part of a larger effort that's underway in the Division to try to make labeling more specific to the indications that were actually studied. . . . We've gradually been shifting from the very general psychotropic claims to looking very specifically at the specific entities that were studied. So focusing in this particular label on schizophrenia is part of that effort. You'll be seeing more of that in the future.

*Id.*

44. *Wyeth v. Levine*, 555 U.S. 555, 568 (2009) ("Generally speaking, a manufacturer may only change a drug label after the FDA approves a supplemental application. There is, however, an FDA regulation that permits a manufacturer to make certain changes to its label before receiving the agency's approval. Among other things, this 'changes being effected' (CBE) regulation provides that if a manufacturer is changing a label to 'add or strengthen a contraindication, warning, precaution, or adverse reaction' or to 'add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product,' it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval." (quoting 21 C.F.R. § 314.70(c)(6)(iii)(A), 314.70(c)(6)(iii)(C) (2009))).

45. See 21 C.F.R. § 202.1(e)(4) (2015) ("An advertisement for a prescription drug . . . shall not recommend *any use that is not in the labeling . . .*" (emphasis added)).

46. See Thomas L. Hafemeister & Sarah P. Bryan, *Beware Those Bearing Gifts: Physicians' Fiduciary Duty to Avoid Pharmaceutical Marketing*, 57 U. KAN. L. REV. 491, 492–500 (2009) (describing the scope and variety of promotion of prescription drugs).

TABLE 1. SPEECH AND CONDUCT CHARACTERIZED AS “PROMOTION” BY THE U.S. DEPARTMENT OF JUSTICE AND FOOD AND DRUG ADMINISTRATION

<i>Designation</i>	<i>Speech</i>	<i>Conduct</i>
<i>Legal</i>	<ul style="list-style-type: none"> <li>• Dissemination of on-label reprints</li> <li>• On-label DTC advertising</li> <li>• On-label in-person detailing</li> <li>• On-label CME programs</li> <li>• Disease awareness campaigns</li> <li>• Using Rx information to inform detailing</li> <li>• Press releases about no-label clinical trials</li> </ul>	<ul style="list-style-type: none"> <li>• Patent “extensions,” (i.e., “me too” products)</li> <li>• Pricing practices (within non-FDA parameters)</li> <li>• Designing and funding research/clinical studies</li> <li>• Sampling</li> <li>• Packaging (single- vs. multi-dose)</li> </ul>
<i>Illegal*</i>	----- Consulting with key opinion leaders -----	
	<ul style="list-style-type: none"> <li>• Press releases about off-label clinical trials</li> <li>• Off-label CME programs</li> <li>• Off-label in-person detailing</li> <li>• Dissemination of off-label reprints</li> <li>• Misrepresentation of clinical data (whether risk/safety or efficacy)</li> <li>• Off-label, “unbalanced” DTC and social media</li> </ul>	<ul style="list-style-type: none"> <li>• Kickbacks for prioritizing products</li> <li>• Hatch-Waxman “reverse payment” settlement agreements</li> </ul>
		<i>*As applied by the DOJ &amp; FDA</i>

For example, promotional speech can include in-person conversations between pharmaceutical company sales representatives and prescribers in their private practices,<sup>47</sup> video news releases (“ready-made news segments produced or sponsored by drug manufacturers and sent to news channels”),<sup>48</sup> meetings between company employees and state Medicaid formulary committees,<sup>49</sup> or “speaker programs” (where pharmaceutical companies have practicing physicians with experience prescribing their products speak with other physicians).<sup>50</sup>

47. *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2659 (2011) (“Pharmaceutical manufacturers promote their drugs to doctors through a process called ‘detailing.’ This often involves a scheduled visit to a doctor’s office to persuade the doctor to prescribe a particular pharmaceutical. Detailers bring drug samples as well as medical studies that explain the ‘details’ and potential advantages of various prescription drugs. Interested physicians listen, ask questions, and receive followup data.”).

48. Nathan Cortez, *Can Speech by FDA-Regulated Firms Ever Be Noncommercial?*, 37 AM. J.L. & MED. 388, 418 (2011).

49. *See, e.g.*, Settlement Agreement at 3–4, *United States ex rel. Torres v. Shire Specialty Pharm.*, No. 08-4795 (E.D. Pa. Sept. 19, 2014), [http://www.justice.gov/usao/pae/News/2014/September/shire\\_settlementagreement.pdf](http://www.justice.gov/usao/pae/News/2014/September/shire_settlementagreement.pdf) (describing an instance in which Shire sales representatives made false statements about the efficacy of a drug to Medicaid formulary committees).

50. *E.g.*, *United States v. Caronia*, 703 F.3d 149, 156 (2d Cir. 2012) (“Speaker programs enlist physicians, for pay, to speak to other physicians about FDA-approved drug use.”); *Criminal Information* at 29, *United States v. Eli Lilly & Co.*, Cr. No. 09-020 (E.D. Pa. Jan. 15, 2009) (involving Eli

It may also include press releases on ongoing or completed studies of off-label uses,<sup>51</sup> “manufacturer dissemination to physicians of independent medical and scientific publications concerning the off-label uses of their products, . . . manufacturer support for Continuing Medical Education (CME) programs for doctors that focus on off-label uses,”<sup>52</sup> and manufacturer dissemination of clinical practice guidelines.<sup>53</sup>

Additionally, promotional conduct can include the provision of free drug samples to prescribers (i.e., “sampling”),<sup>54</sup> pricing practices, manufacturing and packaging decisions,<sup>55</sup> the use of intellectual property laws to postpone the entrance of generic competitors<sup>56</sup> or the release of “me too” products, contact with “key opinion leader[s]” (and paying for the flights, hotels, and meals related to meetings with company employees),<sup>57</sup> or payments to prescribers and pharmacy benefit managers to prioritize certain products.<sup>58</sup> Given the varied universe of speech and conduct bundled into the term “off-label promotion,” it is naïve to assume that First Amendment analysis of one form of off-label communication is representative of all promotional activities.<sup>59</sup>

#### B. *Off-Label Promotion Might Render an FDA-Approved Drug “New”*

Off-label promotion by pharmaceutical companies, whether in the form of speech or conduct, is considered evidence of an intended use of a drug in viola-

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Lilly physicians who were trained as sales representatives to promote Zyprexa on behalf of the company).

51. *E.g.*, *United States v. Harkonen*, No. C 08–00164 MHP, 2009 WL 1578712, at \*6 (N.D. Cal. June 4, 2009).

52. *Wash. Legal Found. v. Henney*, 202 F.3d 331, 333 (D.C. Cir. 2000).

53. FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 14.

54. Hafemeister & Bryan, *supra* note 46, at 495–96.

55. *See, e.g.*, Barry Meier, *New Dosages of Old Drugs Help Raise Their Prices*, N.Y. TIMES, Feb. 10, 2015, at B1 (“[D]octors who . . . dispense the drugs they prescribe directly to patients have recently embraced a new pill that contains 7.5 milligrams of the muscle relaxant. There is no evidence to suggest that the pill works any better except, perhaps, for doctors and the middlemen supplying them. They can charge \$3.45, or about five times as much as a five- or 10-milligram pill.”).

56. *See, e.g.*, *F.T.C. v. Actavis, Inc.*, 133 S. Ct. 2223, 2225 (2013) (explaining that Hatch-Waxman “reverse payment” settlement agreements between branded and generic pharmaceutical companies postpone entrance of generic competitor products).

57. *See* U.S. FOOD & DRUG ADMIN., GUIDANCE INDUSTRY: RESPONDING TO UNSOLICITED REQUESTS FOR OFF-LABEL INFORMATION ABOUT PRESCRIPTION DRUGS AND MEDICAL DEVICES 5 (2011), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm285145.pdf> [hereinafter FDA, RESPONDING TO UNSOLICITED REQUESTS].

58. *See, e.g.*, Third Amended Complaint of Qui Tam Plaintiff Bernard Lisitza at 28–36, *U.S. ex rel. Lisitza v. Johnson & Johnson*, 765 F. Supp. 2d 112 (D. Mass. 2011) (No. 07CV10288), 2010 WL 6845842 (alleging payments made to pharmacy benefit manager to prioritize manufacturer’s products).

59. *See* A. Elizabeth Blackwell & James M. Beck, *Drug Manufacturers’ First Amendment Right to Advertise and Promote Their Products for Off-Label Use: Avoiding a Pyrrhic Victory*, 58 FOOD & DRUG L.J. 439, 447 (2003) (“Under this definition of commercial speech, it is likely that FDA policies restrict not only commercial speech, but also a great deal of core scientific expression regarding off-label use.”).

tion of the “new drug” provisions of the FDCA.<sup>60</sup> The FDA has the authority to regulate “drugs” as defined by the FDCA.<sup>61</sup> Specifically (for purposes of this analysis), the FDA is charged with ensuring that “[n]o person shall introduce or deliver for introduction into interstate commerce *any new drug*, unless an approval of an application filed . . . [with the FDA] is effective with respect to such drug.”<sup>62</sup> A violation of this provision results in a strict liability criminal misdemeanor, punishable by imprisonment for not more than one year or a fine not exceeding \$1,000, or both.<sup>63</sup>

A “new drug” is defined as “[a]ny drug . . . not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof.”<sup>64</sup> As the FDA’s legal theory goes, when a pharmaceutical company promotes a drug for an off-label use, the promotion inherently alters the contents of the “labeling” to include a use or condition for which the drug is “not generally recognized . . . as safe and effective.”<sup>65</sup> Every subsequent shipment and sale of this “new” (and yet already approved) drug in interstate commerce is a violation of the FDCA until the company files, and the FDA approves, a supplemental new drug application.<sup>66</sup>

The statutory definition of “drug” includes an “article[] *intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals*”<sup>67</sup> and an “article[] (other than food) *intended to affect the structure or any function of the body of man or other animals.*”<sup>68</sup> For purposes of identifying and alleging an “intended use,” the government does not distinguish between an internal marketing strategy (regardless of whether any communication of these possible uses to prescribers outside the organization has actually occurred) and external sales training or detailing documents (i.e., those explicitly created for communication with external prescribers). Evidence of a manufacturer’s intended uses may be determined through

such persons’ expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or

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60. United States v. Caronia, 703 F.3d 149, 154–55 (2d Cir. 2012).

61. 21 U.S.C.A. § 321(g) (West 2015) (defining the term “drug”).

62. *Id.* § 355(a) (emphasis added).

63. *Id.* § 331(d) (making it a “prohibited act” to introduce a new drug into interstate commerce in violation of 21 U.S.C.A. § 355); *id.* § 333(a)(1) (creating a strict liability misdemeanor for any violation of 21 U.S.C.A. § 331).

64. *Id.* § 321(p).

65. FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 5 n.16 (providing that “a drug is a new drug if it is not generally recognized as ‘safe and effective’ for its intended uses”).

66. See *id.* at 4 n.13 (“Introducing an unapproved new drug into interstate commerce is prohibited.”).

67. 21 U.S.C.A. § 321(g)(1)(B) (emphasis added).

68. *Id.* § 321(g)(1)(C) (emphasis added).

written statements by such persons or their representatives. It may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised. The intended uses of an article may change after it has been introduced into interstate commerce by its manufacturer. If, for example, a packer, distributor, or seller intends an article for different uses than those intended by the person from whom he received the drug, such packer, distributor, or seller is required to supply adequate labeling in accordance with the new intended uses. But if a manufacturer knows, or has knowledge of facts that would give him notice, that a drug introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a drug which accords with such other uses to which the article is to be put.<sup>69</sup>

Congress has, in the past, exempted certain types of off-label promotion from being considered as evidence of the manufacturer's "intended uses"—specifically, the "disseminat[ion] [of] medical and scientific information that discusses unapproved uses of approved drugs to 'health care professionals and certain entities, including pharmacy benefits managers, health insurance issuers, group health plans, and Federal or State governmental agencies.'" <sup>70</sup> Dissemination was allowed, though, only for uses already in the pipeline for FDA approval.<sup>71</sup> This provision was allowed to sunset in 2006.<sup>72</sup> Merely studying an unapproved new use for an already FDA-approved drug may render the drug "investigational," and potentially trigger the statutory and regulatory provisions governing Investigational New Drug applications.<sup>73</sup>

More recently, the FDA has issued nonbinding guidances suggesting that if pharmaceutical companies disseminate materials consistent with those guidanc-

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69. 21 C.F.R. § 201.128 (2015).

70. FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 5 (discussing the Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296).

71. Food and Drug Administration (FDA) Modernization Act of 1997, Pub. L. 105-115, § 401, 111 Stat. 2296.

72. FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 6.

73. *Off-Label and Investigational Use of Marketed Drugs, Biologics, and Medical Devices—Information Sheet*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126486.htm> (last updated June 25, 2014) ("'Investigational use' suggests the use of an approved product in the context of a clinical study protocol [see 21 CFR 312.3(b)]. When the principal intent of the investigational use of a test article is to develop information about the product's safety or efficacy, submission of an IND or IDE may be required."); *see also* 21 C.F.R. § 312.7(a) ("A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.").

es, the agency "does not intend to use such distribution as evidence of the manufacturer's intent that the product be used for an unapproved new use."<sup>74</sup> One of the FDA's conditions for dissemination is that all reprints "[b]e distributed separately from the delivery of information that is promotional in nature."<sup>75</sup>

For example, if a sales representative delivers a reprint to a physician in his or her office, the reprint should not be attached to any promotional material the sales representative uses or delivers during the office visit. To the extent that the recipients of the scientific or medical journal article have questions, the sales representative should refer the questions to a medical/scientific officer or department, and the officer or department to which the referral is made should be independent of the sales and/or marketing departments. Similarly, while reprints may be distributed at medical or scientific conferences in settings appropriate for scientific exchange, reprints should not be distributed in promotional exhibit halls or during promotional speakers' programs.<sup>76</sup>

Unlike these slightly safer harbors for disseminating off-label information, "if during a sales call to a physician, a sales representative summarizes or characterizes the article to emphasize portions of the article that suggest the manufacturer's drug may be safe or effective for an unapproved use, this might be used as evidence of intended use."<sup>77</sup>

The FDA suggests that the need to establish safety and efficacy for each new use comes from

experience showing that exclusive reliance on post-hoc remedies, such as enforcement actions for false or misleading labeling, was inadequate to protect the public health, as these remedies were not sufficient to deter manufacturers and distributors—who profit from sales of their products for any use—from making unsubstantiated and misleading claims to encourage use of their products.<sup>78</sup>

While this may be true, the "experience" which the agency cites for this proposition dates back to 1962 when Congress first required manufacturers to demonstrate a drug's efficacy to earn FDA approval.<sup>79</sup> Prior to that time, there were no requirements for manufacturers to show that their drugs *worked at all*.<sup>80</sup>

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74. FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 6; *see also* FDA, RESPONDING TO UNSOLICITED REQUESTS, *supra* note 57, at 3 ("FDA does not intend to use such responses as evidence of the firm's intent that the product be used for an unapproved or uncleared use.").

75. FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 8.

76. *Id.*

77. *Id.* at 9.

78. *Id.* at 3 n.9.

79. *Id.* ("As the Secretary of Health, Education, and Welfare told Congress, '[i]t is intolerable to permit the marketing of worthless products under the rules of a cat-and-mouse-game where a manufacturer can fool the public until the [FDA] finally catches up with him.'" (alterations in original) (quoting *The Drug Industry Antitrust Act of 1962: Hearings Before the Antitrust Subcomm. of the Comm. on the Judiciary*, 87th Cong., 2d Sess. 171 (1962) (statement of Abraham A. Ribicoff, Secretary of Health, Education, and Welfare))).

80. HUTT ET AL., *supra* note 23, at 643.

Today's current system of premarket approval and postmarket pharmacosurveillance (not to mention medical practice) is radically different from the system fifty years ago.

C. *Off-Label Promotion May Result in a "Misbranded" Product*

It is a violation of the FDCA to introduce "misbranded" drugs into interstate commerce.<sup>81</sup> Efforts to combat off-label promotion have relied on two theories of misbranding: (1) failure to provide adequate directions for use, and (2) false or misleading labeling.

1. Adequate Directions for Intended Use

The U.S. Department of Justice (in its representation of the FDA) has concluded that "[a]n approved drug that is marketed for an unapproved use (whether in labeling or not) is misbranded because the labeling of such drug does not include 'adequate directions for use.'"<sup>82</sup> In doing so, "the government has treated promotional speech as more than merely evidence of a drug's intended use—it has construed the FDCA to prohibit promotional speech as misbranding itself."<sup>83</sup>

This interpretation endures despite the fact the FDCA and supporting regulations suggest that prescription drugs are exempt from needing "adequate directions for use."<sup>84</sup> Section 502 of the FDCA (codified at 21 U.S.C. 352(f)) is the statutory requirement that drug labels should contain "adequate directions for use."<sup>85</sup> The FDCA explicitly states that prescription drugs "shall be exempt from the requirements of section 502 [of the FDCA]."<sup>86</sup> Instead of requiring adequate directions for use, the FDCA requires prescription drugs to "bear[], at a minimum, the symbol 'Rx only.'"<sup>87</sup>

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81. 21 U.S.C.A. § 331(a) (West 2015).

82. *United States v. Caronia*, 703 F.3d 149, 155 (2d Cir. 2012) (alteration in original) (quoting FDA, *Good Reprint Practices*, *supra* note 7).

83. *Id.*

84. *See* 21 U.S.C.A. § 353(b)(2) ("Any drug dispensed by filling or refilling a written or oral prescription of a practitioner licensed by law to administer such drug shall be exempt from the requirements of section 352 of this title . . .").

85. *See, e.g., Caronia*, 703 F.3d at 154 ("The FDCA prohibits 'misbranding,' or '[t]he introduction or delivery for introduction into interstate commerce of any . . . drug . . . that is . . . misbranded.' A drug is misbranded if, *inter alia*, its labeling fails to bear 'adequate directions for use,' which FDA regulations define as 'directions under which the lay [person] can use a drug safely and for the purposes for which it is intended.'" (alterations in original) (ellipses in original) (citations omitted)). To her credit, Judge Livingston recognized in her dissenting opinion that these exemptions existed, but *Caronia's* counsel apparently did not claim the exemption for *Xyrem*. *Id.* at 181 n.1 (Livingston, J., dissenting); *see also* Guilty Plea Agreement at 5, *United States v. Eli Lilly & Co.*, Cr. No. 09-020 (E.D. Pa. Jan. 15, 2009) (Eli Lilly plead guilty to violating 21 U.S.C.A. § 352(f)(1), admitting that "Zyprexa's labeling did not bear adequate directions for each of the drug's intended uses").

86. Durham-Humphrey Amendment, Pub. L. No. 82-215, 65 Stat. 648, 649 (1951).

87. *See* 21 U.S.C.A. § 353(b)(4)(A) (discussing the "Rx only" requirement).

Consistent with the statutory exemption, the FDA's own regulations<sup>88</sup> provide that prescription drugs<sup>89</sup> are exempt from the requirement to provide adequate directions for use such that a "layman can use a drug safely and for the purposes for which it is intended."<sup>90</sup> Instead, FDA prescription drugs need only a statement of "Rx only," the drug name, "the recommended or usual dosage," "the route of administration, if it is not for oral use," and "the quantity or proportion of each active ingredient."<sup>91</sup> Even so, federal prosecutors still include misbranding due to lack of adequate directions for use in their summary of violations triggered by off-label promotion.<sup>92</sup>

Although this provision is relied upon by the government and industry to craft settlement agreements resolving complicated and expensive investigations into allegations of off-label promotion that do not trigger mandatory exclusion from the Medicare program,<sup>93</sup> a complete reading of the FDCA makes it clear that prescription drugs are, in fact, exempt from this requirement.<sup>94</sup>

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88. See 21 C.F.R. § 201.100(b) (2015).

89. 21 U.S.C.A. § 353(b)(1)(A) (drugs which "because of [their] toxicity or other potentiality for harmful effect, or the method of [their] use, or the collateral measures necessary to [their] use, [are] not safe for use except under the supervision of a practitioner licensed by law to administer such drug[s]").

90. 21 C.F.R. § 201.5.

91. *Id.* § 201.100(b).

92. *E.g.*, Government's Memorandum for Entry of Plea and Sentencing at 2–4, *United States v. Cephalon, Inc.*, No. 2:08-cr-00598 (E.D. Pa. Oct. 10, 2008).

93. See 42 U.S.C. § 1320a-7(a) (2012) (mandatory exclusion); *id.* § 1320a-7(b)(7) (2015) (permissive exclusion for fraud and kickbacks). See *generally Exclusions Program*, OFFICE OF INSPECTOR GEN., U. S. DEP'T OF HEALTH & HUMAN SERVS., <http://oig.hhs.gov/fraud/exclusions.asp> (last visited Nov. 1, 2015) (providing background information on the exclusions program); Stephanie L. Trunk, Note, *Sounding the Death Toll for Health Care Providers: How the Civil False Claims Act Has a Punitive Effect and Why the Act Warrants Reform of its Damages and Penalties Provision*, 71 GEO. WASH. L. REV. 159, 161 (2003) ("Providers who are found to have submitted false claims or settle false claims may also be subject to exclusion from the Medicare program under Title IX of the Social Security Act.").

94. Query what roles and purposes of law are undermined when regulators and regulated industries misinterpret law to their mutual benefit (but at the cost of less transparency, no meaningful public fact-finding, and no third-party review/application of the law). Recently, this misinterpretation has been raised as part of a complaint seeking declaratory and injunctive relief against the FDA because of the "Catch-22" it has created for pharmaceutical companies. Complaint for Declaratory and Injunctive Relief at 19, *Pacira Pharmaceuticals, Inc. v. U.S. Food & Drug Admin.*, No. 1:15-cv-07055 (S.D.N.Y. filed Sept. 8, 2015), 2015 WL 5256628 ("FDA's regulations effectively create a Catch-22 for pharmaceutical manufacturers. On one hand, manufacturers are required to include in product labeling detailed information about all intended uses, including those that are off-label, to avoid a misbranding charge based on a lack of 'adequate directions for use.' On the other hand, under the 'new drug' rationale described above, manufacturers are prohibited from supplementing or revising the product labeling without FDA approval. FDA relies on this construct, which does not appear in the FDCA, to restrict pharmaceutical manufacturers such as Pacira from conveying to sophisticated health care professionals virtually any information—regardless of its quality or veracity—that differs from the FDA-approved product labeling or that is not supported by evidence meeting FDA's strict 'substantial evidence' standard.").

## 2. False or Misleading Labeling

A drug may be considered misbranded, too, “[i]f its labeling is false or misleading in any particular.”<sup>95</sup> Unlike the new drug and misbranding theories that rely upon off-label promotional efforts as evidence of an unapproved “intended use” (arguably incidental, content-neutral restrictions on expression of scientific and medical information), this provision of the FDCA directly restricts written communication of information pertaining to a product.<sup>96</sup>

In considering whether a product is misbranded because the labeling or advertising is misleading, the FDA is explicitly allowed to consider

not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof.<sup>97</sup>

Off-label promotion of drugs tends to focus on the potential benefits of drugs for patients and conditions otherwise excluded from the studies considered and approved by the FDA as part of the labeling. Discussion of these benefits may be based upon smaller clinical studies, observational studies, anecdotal case reports, or emerging data from ongoing clinical studies eventually used to support additional on-label indications for the drug. While some argue that off-label promotion is inherently misleading<sup>98</sup> (or that the burden of proving “truth” should be borne by manufacturers),<sup>99</sup> courts have disagreed and found attempts to restrict truthful, not misleading off-label speech in violation of the First Amendment.<sup>100</sup>

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95. 21 U.S.C.A. § 352(a) (West 2015).

96. See *Kordel v. United States*, 335 U.S. 345, 347–48 (1948) (“[L]abeling is defined in § 201(m) to mean ‘all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article.’” (footnote omitted)).

97. 21 U.S.C.A. § 321(n).

98. E.g., Stephanie M. Greene, *After Caronia: First Amendment Concerns in Off-Label Promotion*, 51 SAN DIEGO L. REV. 645, 690 (2014) (“A common sense approach to the issue of off-label detailing is arguing the practice is inherently misleading.”).

99. E.g., Christopher Robertson, *When Truth Cannot Be Presumed: The Regulation of Drug Promotion Under an Expanding First Amendment*, 94 B.U. L. REV. 545, 569 (2014) (“Here, however, the present question is distinct: Who should have the burden when the truthfulness is unknown? That question is unsettled, but could be resolved in a way that places the burden on drugmakers for off-label promotional claims.”).

100. See, e.g., *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 67 (D.D.C. 1998), *amended by* 36 F. Supp. 2d 16 (D.D.C. 1999), *appeal dismissed, judgment vacated in part sub nom.* *Wash. Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000) (“In asserting that any and all scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs are presumptively untruthful or misleading until the FDA has had the opportunity to evaluate them, FDA exaggerates its overall place in the universe. It is certainly the case that by statute, no drug may be introduced or delivered into interstate commerce without FDA approval, and that the claims that a manufacturer may make about a drug through labeling, advertising and other forms of promotion are subject to FDA regulatory authority. However, the conclusions reached by a laboratory scientist or

## II. WHAT MAKES SPEECH COMMERCIAL?

Commercial speech is "usually defined as speech that does no more than propose a *commercial transaction*"<sup>101</sup> and is "linked inextricably with the commercial arrangement that it proposes."<sup>102</sup> And what is a commercial transaction? A "transaction" requires an agreement or exchange that "involve[es] two or more persons,"<sup>103</sup> and "commerce" requires an "exchange of goods or services."<sup>104</sup> In other words, a commercial transaction requires an exchange of goods or services involving two or more persons. Speech that "*does no more than propose a commercial transaction*" is limited, then, to speech that discusses, encourages, or informs the possible exchange of goods or services between two or more persons, a potential buyer and seller.<sup>105</sup> What to do, then, with a conversation with someone who is not in a position to purchase the product being discussed, who faces potential criminal charges if she proposes or receives remuneration for her services (i.e., prescribing the product), and who owes another a fiduciary duty to exercise independent professional judgment in the other's best interest?

"[T]he general rule is that the speaker *and the audience*, not the government, assess the value of the information presented."<sup>106</sup> The assumption that dissemination and discussion of off-label use of prescription drugs is inherently

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university academic and presented in a peer-reviewed journal or textbook, or the findings presented by a physician at a CME seminar are not 'untruthful' or 'inherently misleading' merely because the FDA has not yet had the opportunity to evaluate the claim.").

In *Thompson v. Western States Medical Center*, pharmacists successfully used the First Amendment to challenge a federal statute prohibiting advertising and promotion of compounded drugs. 535 U.S. 357 (2002). Compounded drugs are inherently off-label because they are exempt from the FDA's standard drug approval requirements. 21 U.S.C.A. § 353(a). As a result, compounded drugs do not have the same FDA-approved labeling required for the sale of most prescription drugs. In *Thompson*, the government did not argue that the advertising and promotion of compounded drugs would be misleading. *Thompson*, 535 U.S. at 368. Both parties to this case agreed that the advertising and soliciting prohibited constituted commercial speech, so the question of whether communications with prescribers were, in fact, commercial was neither raised nor addressed by the Court. *Id.* at 366.

101. *United States v. United Foods, Inc.*, 533 U.S. 405, 409 (2001) (emphasis added) (citing *Va. Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 762 (1976)).

102. *Edenfield v. Fane*, 507 U.S. 761, 767 (1993); *see also* *Friedman v. Rogers*, 440 U.S. 1, 10 n.9 (1979) ("By definition, commercial speech is linked inextricably to commercial activity: while the First Amendment affords such speech 'a limited measure of protection,' it is also true that 'the State does not lose its power to regulate commercial activity deemed harmful to the public whenever speech is a component of that activity.'" (quoting *Ohralik v. Ohio State Bar Ass'n*, 436 U.S. 447, 456 (1978))).

103. *Transaction*, BLACK'S LAW DICTIONARY (7th ed. 1999).

104. *Commerce*, BLACK'S LAW DICTIONARY (7th ed. 1999).

105. *Edenfield*, 507 U.S. at 767 (emphasis added); *id.* at 766 ("In the commercial context, solicitation may have considerable value. Unlike many other forms of commercial expression, solicitation allows direct and spontaneous communication *between buyer and seller*." (emphasis added)); *see also* *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557, 561 (1980) ("[C]ommercial speech . . . is[] expression related solely to the economic interests of *the speaker and its audience*." (emphasis added)).

106. *United Foods, Inc.*, 533 U.S. at 411 (alteration in original) (emphasis added) (quoting *Edenfield*, 507 U.S. at 767).

commercial speech has been grounded primarily in the speaker's intent<sup>107</sup> and has not considered the audience's position or role. As I argue below, the legal and professional framework in which prescribers are situated relative to pharmaceutical company representatives calls into question whether their conversations and correspondence are correctly characterized as no more than "commercial" in nature.

A. *Speaker Intent as Reflected by Content and Motivation*

In distinguishing commercial from noncommercial speech, the Court has considered whether speakers acted with noncommercial intent "to editorialize on any subject, cultural, philosophical, or political,"<sup>108</sup> or "to report any particularly newsworthy fact, or to make generalized observations even about commercial matters,"<sup>109</sup> or whether "[h]is purpose is strictly business."<sup>110</sup> Unlike noncommercial speakers, commercial speakers who have "strong financial incentive[s] to educate the market and stimulate demand for [their] product[s] or service[s]" want to "discuss and negotiate the desired form for the transaction or professional relation," and hope to "direct [their] proposals toward those consumers who [they have] a reason to believe would be most interested in what [they have] to sell."<sup>111</sup> Even so, "[i]t is not clear that a professional's speech is necessarily commercial whenever it relates to that person's financial motivation for speaking."<sup>112</sup>

Indeed, the critical distinction between the merely commercial speech in *Valentine v. Chrestensen*<sup>113</sup> and the noncommercial speech at issue in *New York Times v. Sullivan*<sup>114</sup> was that the paid advertisement in *Sullivan* "communicated information, expressed opinion, recited grievances, protested claimed abuses, and sought financial support on behalf of a movement whose existence and objectives [were] matters of the highest public interest and concern."<sup>115</sup>

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107. See Cortez, *supra* note 48, at 407 ("The speaker's motives are perhaps the most important factor in determining whether the speech is commercial or not.").

108. *Friedman v. Rogers*, 440 U.S. 1, 11 (1979) (quoting *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 761 (1976)). In *Virginia Citizens Consumer Council*, the Court explained that the communication, "I will sell you the X prescription drug at the Y price," was purely commercial. *Virginia Citizens Consumer Council*, 425 U.S. at 761.

109. *Friedman*, 440 U.S. at 11 (quoting *Va. Citizens Consumer Council, Inc.*, 425 U.S. at 761).

110. *Id.* In *Friedman*, the Court declared the optometrists' use of trade names as "strictly business . . . a form of commercial speech and nothing more." *Id.*

111. *Edenfield*, 507 U.S. at 766.

112. *Riley v. Nat'l Fed'n of the Blind of N.C., Inc.*, 487 U.S. 781, 795 (1988) (citing *Bigelow v. Virginia*, 421 U.S. 809, 826 (1975) (explaining that state labels cannot be dispositive of First Amendment protection)).

113. *Valentine v. Chrestensen*, 316 U.S. 52, 54 (1942) (holding that a city ordinance banning the distribution of handbills advertising submarine tours was constitutional because "the Constitution imposes no such restraint on government as respects purely commercial advertising").

114. *New York Times Co. v. Sullivan*, 376 U.S. 254, 266 (1964) (holding that an editorial advertisement on behalf of black right-to-vote movement was not commercial speech).

115. *Id.* at 266 (citing *NAACP v. Button*, 371 U.S. 415, 435 (1963)).

Later, in *Bolger v. Youngs Drug Products Corp.*,<sup>116</sup> when a condom manufacturer mailed pamphlets to the public that both promoted its products and discussed means of preventing sexually transmitted diseases, the pamphlets were not considered "merely as proposals to engage in commercial transactions."<sup>117</sup> The Court specifically identified the informational pamphlets<sup>118</sup> mailed by Youngs Drug Products as "a closer question," despite the fact that both parties conceded that they were, in fact, advertisements.<sup>119</sup> In its analysis, the Court recognized three characteristics which tend to suggest that speech is commercial, none of which is determinative on its own: (1) the litigants' agreement that the speech is a form of advertisement,<sup>120</sup> (2) reference to a specific product,<sup>121</sup> and (3) the speaker's economic motivation for mailing the pamphlets.<sup>122</sup> It was only "[t]he combination of *all* these characteristics" that "provid[ed] strong support for the . . . conclusion that the informational pamphlets [were] properly characterized as commercial speech."<sup>123</sup>

Later still, when evaluating a restriction on speech in state university dormitories, the Court provided more examples of speech uttered "for a profit" yet considered noncommercial, including "tutoring, legal advice, and medical consultation provided (for a fee) in students' dormitory rooms."<sup>124</sup> While each of these types of speech could be considered "speech for a profit," the Court clarified that, unlike the speech during the Tupperware parties directly at issue in the case, these other examples did not "consist of speech that *proposes* a commercial

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116. *Bolger v. Youngs Drug Prods. Corp.*, 463 U.S. 60 (1983).

117. *Id.* at 66.

118. *Id.* at 62 n.4 ("The first, entitled 'Condoms and Human Sexuality,' [was] a 12-page pamphlet describing the use, manufacture, desirability, and availability of condoms, and providing detailed descriptions of various Trojan-brand condoms manufactured by Youngs. The second, entitled 'Plain Talk about Venereal Disease,' [was] an eight-page pamphlet discussing at length the problem of venereal disease and the use and advantages of condoms in aiding the prevention of venereal disease. The only identification of Youngs or its products [was] at the bottom of the last page of the pamphlet, which states that the pamphlet has been contributed as a public service by Youngs, the distributor of Trojan-brand prophylactics.").

119. *Id.* at 66.

120. *Id.* ("The mere fact that these pamphlets are conceded to be advertisements clearly does not compel the conclusion that they are commercial speech." (citing *New York Times Co.*, 376 U.S. at 265-66)).

121. *Id.* ("[T]he reference to a specific product does not by itself render the pamphlets commercial speech." (citing *Associated Students for Univ. of Cal. at Riverside v. Att'y Gen. of the U.S.*, 368 F. Supp. 11, 24 (C.D. Cal. 1973))).

122. *Id.* at 67 (first citing *Bigelow v. Virginia*, 421 U.S. 809, 818 (1975); then citing *Ginzburg v. United States*, 383 U.S. 463, 474 (1966); and then citing *Thornhill v. Alabama*, 310 U.S. 88 (1940)); *see also* *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557, 559-60 (1980) (explaining that the Public Service Commission of the State of New York found advertising encouraging more consumption commercial, where informational advertising that did not seek to increase aggregate consumption was treated as noncommercial).

123. *Bolger*, 463 U.S. at 67.

124. *Bd. of Trs. of State Univ. of N.Y. v. Fox*, 492 U.S. 469, 482 (1989).

transaction.”<sup>125</sup> Indeed, the Court recognized that “[s]ome of our most valued forms of fully protected speech are uttered for a profit.”<sup>126</sup>

It would appear, then, that one way of distinguishing between commercial and noncommercial speech is whether a speaker intends to provide continued education or a professional consultation (independent of the terms or form of commercial transaction or relationship), or whether the speech is part of a larger negotiation of terms for the potential or likely purchase of goods or services driven solely by “economic self-interest.”<sup>127</sup>

*B. Listener Role as Potential Consumer, Rather than Voter, Student, Client, or Patient*

First Amendment protections apply to both speakers and listeners.<sup>128</sup> Examples of financially interested yet noncommercial speech identified by the Supreme Court have included editorial advertisements by political action groups,<sup>129</sup> inserts sent with utility bills expressing the utility companies’ “opinions or viewpoints on controversial issues of public policy,”<sup>130</sup> as well as “tutoring, legal advice, and medical consultation provided (for a fee).”<sup>131</sup> How does this speech differ from attorney advertising that provides information on “the legal rights of persons injured by the Dalkon Shield that, in another context, would be fully protected speech,”<sup>132</sup> pamphlets mailed to the public discussing both the means of preventing sexually transmitted diseases and the specific condoms one could use to do so,<sup>133</sup> or in-person solicitation by attorneys and certified public ac-

125. *Id.*

126. *Id.*

127. *Cent. Hudson Gas*, 447 U.S. at 564 n.6.

128. *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 756 (1976) (“Freedom of speech presupposes a willing speaker. But where a speaker exists, as is the case here, the protection afforded is to the communication, to its source and to its recipients both.” (footnote omitted)); *Griswold v. Connecticut*, 381 U.S. 479, 482 (1965) (“The right of freedom of speech and press includes not only the right to utter or to print, but the right to distribute, *the right to receive, the right to read and freedom of inquiry*, freedom of thought, and freedom to teach . . .” (emphasis added) (citation omitted)); see also Barbara J. Evans, *The First Amendment Right to Speak About the Human Genome*, 16 U. PA. J. CONST. L. 549, 593 (2014) (“[C]ommercial speech doctrine often values speech for its informational function, as opposed to its expressive function. Valuing speech for its informational content implicitly treats audience interests as an important concern.” (footnote omitted)).

129. See e.g., *New York Times Co.*, 376 U.S. at 266 (holding that an editorial advertisement in a for-profit publication on behalf of the black right-to-vote movement was not commercial speech).

130. *Consol. Edison Co. v. Pub. Serv. Comm’n of N.Y.*, 447 U.S. 530, 533 (1980). In *Consolidated Edison*, the Court declined to apply the *Central Hudson* test despite explicit recognition that the test applied to commercial speech. *Id.* at 538 n.5.

131. *Bd. of Trs. of State Univ. of N.Y.*, 492 U.S. at 482.

132. See *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 637 n.7 (1985) (involving an attorney who ran newspaper advertisements publicizing his services to represent women suffering injuries from a contraceptive known as the Dalkon Shield).

133. See *Bolger v. Youngs Drug Prods. Corp.*, 463 U.S. 60, 62, 66 n.13 (1983) (involving a contraceptive manufacturer and distributor that distributed an unsolicited mass mailing about its product to the public).

countants (CPAs) where potential clients are informed of the scope of possible professional relationships,<sup>134</sup> all of which were deemed "commercial"?

While the primary focus of commercial speech analysis for FDA-regulated speech has been the speaker,<sup>135</sup> the larger body of commercial speech doctrine "pays heed" to the listener as well.<sup>136</sup> Speech considered commercial has been consistently received by a potential consumer (i.e., *possible parties to a commercial transaction with, and proposed by, the speaker*).<sup>137</sup> Speech, whether spoken or written, may be used by buyers to evaluate the people offering products or services,<sup>138</sup> to explore products or services in detail,<sup>139</sup> to compare alternative goods and services,<sup>140</sup> to simply initiate a process of consideration,<sup>141</sup> or to "discuss and negotiate the desired form for the transaction or professional relation" with the speaker.<sup>142</sup>

Readers or listeners of the noncommercial speech, by contrast, were in receipt of information upon which they might act to further noncommercial (e.g., political, educational, medical, or legal) interests. In other words, the information was not provided in order to induce a commercial transaction between a speaker and listener, either because the terms and form of the commercial transaction had already been negotiated (as in the case of the tutoring, legal advice, medical consultation, or utility services being billed) or because there was no commercial transaction to propose (e.g., the group advancing voting rights had no goods or services to sell).<sup>143</sup> As explained above, a commercial transaction requires the exchange of goods or services between a seller and a buyer. It

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134. See *Edenfield v. Fane*, 507 U.S. 761, 765 (1993) ("In soliciting potential clients, Fane seeks to communicate no more than truthful, non-deceptive information proposing a lawful commercial transaction."); *Ohralik v. Ohio State Bar Ass'n*, 436 U.S. 447, 455–56 (1978) (involving an attorney's in-person solicitation of a client).

135. See *Cortez*, *supra* note 48, at 407 ("The speaker's motives are perhaps the most important factor in determining whether the speech is commercial or not.").

136. *Evans*, *supra* note 128, at 593 ("The commercial speech doctrine pays heed to the interests of listeners.").

137. *Edenfield*, 507 U.S. at 765 ("In soliciting potential clients, Fane seeks to communicate no more than truthful, non-deceptive information proposing a lawful commercial transaction."); see also *Gordon & Breach Sci. Publishers S.A. v. Am. Inst. of Physics*, 859 F. Supp. 1521, 1544 (S.D.N.Y. 1994) (holding that nonprofit scientific societies' distribution of journal article preprints at a librarians' conference and continued dissemination of survey results favoring the societies' publications to "an audience that represents the core consumers of those products" was commercial speech).

138. *Edenfield*, 507 U.S. at 766.

139. *Id.*

140. *Id.*

141. *Id.* at 775–76.

142. *Id.* at 766.

143. See *Ohralik v. Ohio State Bar Ass'n*, 436 U.S. 447, 458 (1978) ("But neither of the Disciplinary Rules here at issue prohibited appellant from communicating *information* to these young women about their legal rights and the prospects of obtaining a monetary recovery, or from recommending that they obtain counsel. [The Rule] merely prohibited him from using the information as *bait* with which to obtain an agreement to represent them for a fee." (emphasis added)).

should follow, then, that speech doing no more than proposing a commercial transaction must be between potential sellers and buyers (or their agents).<sup>144</sup>

### III. THE COURTS APPLYING THE FIRST AMENDMENT TO THE GOVERNMENT'S ATTEMPTS TO RESTRICT OFF-LABEL "PROMOTION" HAVE TENDED TO IGNORE THE ROLE OF THE LISTENER IN THE ANALYSIS.

In the past twenty years, federal courts have considered the First Amendment implications of the FDA's attempts to restrict off-label promotion of prescription drugs by pharmaceutical companies in two contexts: first, in a facial challenge by the Washington Legal Foundation (WLF) to the FDA's policy statements limiting dissemination of "enduring materials" (reprints of medical journal articles, clinical practice guidelines, and textbooks) and industry sponsorship of continuing medical education programs in which off-label uses were discussed;<sup>145</sup> and second, as applied in criminal cases threatened<sup>146</sup> or brought by the federal government against individuals working for pharmaceutical companies for engaging in speech about off-label uses of their products.<sup>147</sup> These courts have generally ignored the role of listener intent in determining whether speech is commercial, despite it being both supported by the existing body of law, and critical to accurate assessment of discussion and dissemination of off-label information.

Assessments in "as-applied" cases have relied heavily on the First Amendment analysis in the District Court for the District of Columbia's opinion discussing the facial challenge by the WLF,<sup>148</sup> as have the majority of courts that have

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144. See *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557, 561 (1980) ("[C]ommercial speech . . . is[] expression related solely to the economic interests of the speaker and its audience." (emphasis added)).

145. *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 54 (D.D.C. 1998), amended by 36 F. Supp. 2d 16 (D.D.C. 1999), appeal dismissed, judgment vacated in part *sub nom.* *Wash. Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000).

146. *Amarin Pharma, Inc. v. U.S. Food & Drug Admin.*, No. 15 CIV. 3588 (PAE), 2015 WL 4720039, at \*20 (S.D.N.Y. Aug. 7, 2015) ("10 days before Amarin filed suit, the FDA had expressly threatened . . . to bring a misbranding action against it for promoting Vascepa off-label . . .").

147. See *United States v. Harkonen*, No. C 08-00164 MHP, 2009 WL 1578712, at \*5 (N.D. Cal. June 4, 2009); *United States v. Caronia*, 576 F. Supp. 2d 385, 389-90 (E.D.N.Y. 2008), vacated and remanded, 703 F.3d 149 (2d Cir. 2012).

148. E.g., *Caronia*, 576 F. Supp. at 393 ("The seminal case on the FDA's regulation of guidance relating to the off-label use of prescription drugs is Judge Lamberth's decision in *Washington Legal Foundation v. Friedman* . . ."); *Amarin Pharma, Inc.*, 2015 WL 4720039, at \*1 ("This case grows out of the decision in *Caronia* and involves the same misbranding provisions."); *Harkonen*, 2009 WL 1578712, at \*5 (N.D. Cal. June 4, 2009) ("While the FDCA prohibits speech that promotes off-label uses for approved drug products (which thereby 'misbrands' the drug), the government cannot wholesale proscribe the open dissemination of scientific opinions and ideas concerning all beneficial uses for approved drug products. Such a prohibition has been deemed to violate the First Amendment rights of the speakers to communicate scientific information and engage in scientific discourse about such products." (citing *Wash. Legal Found.*, 13 F. Supp. 2d at 74)). Indeed, the court in *Harkonen* only cursorily addressed the *Bolger* factors. See *id.* at \*6. Similarly, the Court of Appeals for the Second Circuit did not independently consider the *Bolger* factors, but rather relied upon the Supreme Court's decision in *Sorrell v. IMS Health*, 131 S. Ct. 2653, 2659 (2011), for the premise that *Caronia's* speech was

indirectly considered the nature of pharmaceutical speech regarding off-label use of their products.<sup>149</sup> Because of the anchoring role that *Washington Legal Foundation v. Friedman*<sup>150</sup> has played in First Amendment analysis of off-label speech by pharmaceutical companies, this Section looks at the district court’s analysis and identifies a number of problematic assumptions made by the court in determining whether the speech at issue was “commercial.”

Two of the factors identified in *Bolger* as potentially indicative of commercial speech are easily satisfied by a manufacturer’s dissemination of information on off-label uses.<sup>151</sup> There is no dispute that manufacturers deliberately disseminate information that refers to specific products out of a well-known economic motivation.<sup>152</sup> Analysis of the third factor, though, warrants a closer look. In determining whether the speech at issue in the WLF litigation was “concededly an advertisement,” the district court decided that continuing medical education (CME) seminars and dissemination of enduring materials satisfied the “commonly understood” dictionary definition of “advertising” because they “call[ed] public attention” to a product, “especially by emphasizing desirable qualities so as to arouse a desire to buy or patronize.”<sup>153</sup> In applying this dictionary definition to the CME seminars and enduring materials at issue, Judge Lamberth equated physician attention to “public attention” and the act of prescribing to “buy[ing] or patroniz[ing].”<sup>154</sup> The district court ultimately found that manufacturer sponsorship of CME seminars and dissemination of enduring materials was commercial speech because CME programs “‘propose a commercial transaction’ . . . [by] suggest[ing] that a physician should prescribe—and a consumer therefore will purchase—the subject drug.”<sup>155</sup>

There are three problematic leaps in this analysis, all of which dismiss the importance of listener intent in First Amendment analysis. First, Congress and

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“[s]peech in aid of pharmaceutical marketing.” *Caronia*, 703 F.3d at 163 (quoting *Sorrell*, 131 S. Ct. at 2659). Of course, *Sorrell* dealt specifically with the purchase and sale of prescriber information collected at the point of sale of a prescription drug, not dissemination of information on off-label use of prescription drugs. *Sorrell*, 131 S. Ct. at 2526.

149. *E.g.*, *Genzyme Corp. v. Shire Human Genetic Therapies, Inc.*, 906 F. Supp. 2d 9, 15 (D. Mass. 2012) (relying on *Washington Legal Foundation* as part of its analysis of whether a pharmaceutical company’s publication and distribution of a press release about an off-label use violated the Lanham Act).

150. *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998), *amended by* 36 F. Supp. 2d 16 (D.D.C. 1999), *appeal dismissed, judgment vacated in part sub nom.* *Wash. Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000).

151. See *supra* notes 120–23 and accompanying text for a delineation of the *Bolger* factors.

152. *Wash. Legal Found.*, 13 F. Supp. at 65 (“[B]ecause this information is in fact supplied by the manufacturer, and because the primary purpose for supplying the information is to encourage the purchase of the featured product, the court must conclude that the speech is ‘entitled to the qualified but nonetheless substantial protection accorded to commercial speech.’” (quoting *Bolger v. Youngs Drug Prods. Corp.*, 463 U.S. 60, 68 (1983))).

153. *Id.* at 64 (quoting *Advertisement*, WEBSTER’S NINTH NEW COLLEGIATE DICTIONARY (9th ed. 1990)).

154. *Id.*

155. *Id.* (quoting *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 762 (1976)).

the FDA have historically recognized conversations between manufacturers and prescribers as distinct from conversations between manufacturers and the public (e.g., direct-to-consumer advertising).<sup>156</sup> In *Bolger*, the pamphlets at issue were broadly distributed to the end consumers.<sup>157</sup> Prescribers, whether physicians, dentists, nurse practitioners, or physician assistants, are all licensed professionals. Their education, licenses, and professional training set them apart from the general public, and the law holds them to a higher level of independent judgment. They, unlike the general public or end consumers, are legally required to independently evaluate the risks and benefits of potential treatments, including prescription drugs.

Second, prescribing a treatment for another is factually, legally, and ethically quite different from merely buying something or patronizing someone. Factually, writing a prescription, by itself, does not require the exchange of any goods or money (unlike buying a product or service, which inherently requires the exchange of money). Legally, prescribers (unlike the general public) are acting as fiduciaries for their patients, putting their patients' interests before their own or else risking significant personal liability and professional discipline in the event of an unexpected outcome.<sup>158</sup> Additionally, in order to serve as the "learned intermediaries" envisioned by products liability law, prescribers need information about both on- and off-label uses of drugs (presumably from the manufacturers—the entity that knows the drug best) about how to prescribe safely and effectively.<sup>159</sup> Ethically, prescribers need to keep their knowledge of treatments, including prescription drugs, current both in regards to the emerging science and their patients' specific circumstances in order to practice their professions consistent with ethical norms.<sup>160</sup> The general consumer has no similar ethical duty. As correctly observed by the district court in *Washington Legal Foundation*,

Typical "commercial speech" is authored and/or uttered directly by the commercial entity that wishes to financially benefit from the message. A purveyor of goods or services makes claim about his products to order to induce a purchase. In this instance, by contrast, the speech that

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156. The Federal Torts Claims Act sets advertising to physicians apart from the standard for false advertising to the public. 15 U.S.C.A. § 55(a)(1) (West 2015) ("No advertisement of a drug shall be deemed to be false if it is disseminated only to members of the medical profession, contains no false representation of a material fact, and includes, or is accompanied in each instance by truthful disclosure of, the formula showing quantitatively each ingredient of such drug."). Similarly, both Congress and the FDA have treated direct-to-consumer advertising very differently from communications between manufacturers and prescribers. HUTT ET AL., *supra* note 23, at 907–23.

157. *Bolger*, 463 U.S. at 62.

158. See Hafemeister & Bryan, *supra* note 46, at 492 ("[T]he most effective way to curtail the potentially deleterious effects of marketing is to recognize that physicians have a fiduciary duty to give the well-being of their patients the highest priority."); see also Aaron S. Kesselheim & Jerry Avorn, *Pharmaceutical Promotion to Physicians and First Amendment Rights*, 358 NEW ENG. J. MED. 1727, 1727 (2008) ("Communication by drug manufacturers to physicians has a unique status in both legal and business terms.").

159. HUTT ET AL., *supra* note 23, at 925.

160. See Mary Lynn Dell, Brigitte S. Vaughan & Christopher J. Kratochvil, *Ethics and the Prescription Pad*, 17 CHILD & ADOLESCENT PSYCHIATRIC CLINICS NORTH AM. 93, 93–94 (2008).

the manufacturers wish to "communicate" is the speech of others—the work product of scientists, physicians and other academics.<sup>161</sup>

Not only is the off-label content often authored by someone other than the pharmaceutical company, the listener/reader's primary legal and ethical duty is not to him or herself, but rather to the patient being treated.

Third, while a prescription may be necessary for a patient's legal purchase of a prescription drug, it is hardly sufficient to prompt a purchase. Judge Lamberth recognized that the chain of causation between prescription and purchase requires a patient to act, but assumed that most patients do so unquestioningly:

The peculiarities of the prescription drug industry make dissemination of scientific research results an especially important and prevalent marketing tool. Though patients are the end-point purchasers of prescription drugs, their choices are constrained by physicians because a patient can only obtain the manufacturer's products with a physician's authorization—a prescription. To the extent that physicians are the gatekeepers to sales, the marketing efforts must be directed at them. That fact, combined with *the reality that a typical patient is unlikely to strongly challenge a physician's recommendation concerning a prescription*, or have the education and background to make informed choices among equally effective treatments, means that the treating physician is going to be target of much of the pharmaceutical industry's attention.<sup>162</sup>

This "reality" predates the barrage of direct-to-consumer advertising on the Internet, broadcast television, and radio. Prior to 1997, direct-to-consumer advertising of prescription drugs was primarily a printed media endeavor.<sup>163</sup> Increasingly, patients are willing to challenge, question, or dismiss their prescriber's advice.<sup>164</sup> Also, while a prescription may be necessary, it may no longer be sufficient for an off-label sale. Many patients decide not to fill prescriptions<sup>165</sup> and third-party-payer scrutiny of prescriptions has increased significantly since

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161. Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51, 62 (D.D.C. 1998), amended by 36 F. Supp. 2d 16 (D.D.C. 1999), *appeal dismissed, judgment vacated in part sub nom.* Wash. Legal Found. v. Henney, 202 F.3d 331 (D.C. Cir. 2000).

162. *Id.* at 63 (emphasis added).

163. HUTT ET AL., *supra* note 23, at 916–17.

164. See Daniel M. Schaffzin, *Warning: Lawyer Advertising May Be Hazardous to Your Health! A Call to Fairly Balance Solicitation of Clients in Pharmaceutical Litigation*, 8 CHARLESTON L. REV. 319, 342 (2014) ("Anecdotal evidence, in the form of both formal survey data and other first-hand reporting from medical professionals, supports the argument that widespread advertising for pharmaceutical litigation negatively impacts patient attitudes toward—and compliance with—physician-prescribed medications.").

165. Michael A. Fischer et al., *Primary Medication Non-Adherence: Analysis of 195,930 Electronic Prescriptions*, 25 J. GEN. INTERNAL MED. 284, 287 (2010) (explaining that 22.5% of e-prescriptions tracked in study went unfilled); Robyn Tamblyn et al., *The Incidence and Determinants of Primary Nonadherence with Prescribed Medication in Primary Care: A Cohort Study*, 160 ANNALS INTERNAL MED. 441, 443 (2014) (reporting that nearly one-third of primary care patients did not fill the prescriptions for the medicines they were prescribed within nine months); see also Lars Osterberg & Terrence Blaschke, *Adherence to Medication*, 353 NEW ENG. J. MED. 487, 490 (2005) (stating that patients may not take up to fifty percent of prescribed drugs).

the creation of the prescription drug benefit program for Medicare in 2003.<sup>166</sup> Additionally, the FDA's authority was expanded in 2007 to give the agency permission to identify drugs that are at particularly high risk of misuse, resulting in patient harm, and limit the dispensing of those drugs to on-label use exclusively.<sup>167</sup> Physicians are no longer the only gatekeepers to prescription products.

In addition to these three flawed assumptions, the *Washington Legal Foundation* district court also assumed, as part of its analysis of whether CMEs and enduring materials were commercial speech, that the financial interests of pharmaceutical companies would likely result in the cherry-picking of favorable evidence for off-label discussion, which would, in turn, result in misleading prescribers that the evidence is stronger than it is.<sup>168</sup> But this concern is not properly considered when determining whether speech is or is not commercial in nature,

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166. DANIEL R. LEVINSON, U.S. DEP'T OF HEALTH & HUMAN SERVS., PRESCRIBERS WITH QUESTIONABLE PATTERNS IN MEDICARE PART D 1-2 (2013), <http://oig.hhs.gov/oei/reports/oei-02-09-00603.pdf> (providing one of four studies looking at prescriptions paid for by Medicare Part D); see also *In re Neurontin Mktg. & Sales Practices Litig.*, 712 F.3d 21, 28-29 (1st Cir. 2013) ("The Kaiser Foundation Health Plan and its subsidiaries do not employ physicians themselves, but have exclusive contractual relationships with regional Permanente Medical Groups ('PMGs'). Each PMG has its own Pharmacy and Therapeutics ('P & T') Committee which manages each PMG's formulary, or list of medications that treating physicians may prescribe. Representatives from both entities sit on the P & T Committees and participate in formulary management. Kaiser Foundation Hospitals has a Drug Information Service ('DIS') that researches and communicates information about drugs, including monographs about new drugs or new drug uses, to physicians and P & T Committees. DIS monographs summarize available evidence—including publicly available evidence and unpublished information obtained from pharmaceutical manufacturers—on drug safety and efficacy, and P & T Committees rely heavily on these monographs in making formulary decisions." (citations omitted)); see generally Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003).

167. 21 U.S.C.A. § 355(p)(1) (West 2015) (discussing Risk Evaluation and Mitigation Strategies). For example, Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) program "is an FDA-required program designed to ensure informed risk-benefit decisions before initiating treatment, and while patients are treated to ensure appropriate use of TIRF medicines." *About, TIRF REMS Access*, <https://www.tirfremssaccess.com/TirfUI/remss/home.action> (last visited Nov. 1, 2015). The program defines its purpose as "mitigat[ing] the risk of misuse, abuse, addiction, overdose and serious complications due to medication errors with the use of TIRF medicines." *Id.*

168. *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 65 (D.D.C. 1998), amended by 36 F. Supp. 2d 16 (D.D.C. 1999), *appeal dismissed, judgment vacated in part sub nom.* *Wash. Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000) ("For any given off-label prescription drug treatment, there may be a wide variety of scientific research data available, some of which concludes that the off-label treatment is effective, some of which concludes that the treatment is not. On other hand, manufacturers will likely only seek to disseminate information that presents their product in a favorable light. That fact, combined with the considerable financial resources available to pharmaceutical companies, means that findings concluding that a drug effectively treats a condition is more likely to reach a physician than studies reaching the opposite conclusion. Therefore, physicians could be led to believe that a certain drug is safe and effective because a manufacturer has found, and aggressively promoted, 'the one' article that supports use of their drug, even if there exists considerable evidence to the contrary. The potential to mislead, and the harm that could result, convinces this court that it is permissible to 'depart from the rigorous review that the First Amendment generally demands.'" (footnote omitted)).

rather only after determining that the test in *Central Hudson Gas & Electric Corp. v Public Service Commission of New York*<sup>169</sup> should apply.<sup>170</sup>

Because of the role of listener intent in determining whether speech is commercial, the critical distinctions between prescribers and the general public, and the differences between prescribing a drug and purchasing a drug, it makes sense to revisit the question of whether the dissemination of truthful information about off-label use of prescription drugs should be considered mere advertising.

#### IV. OFF-LABEL “PROMOTION” IS NOT ALWAYS OR INHERENTLY COMMERCIAL IN NATURE.

The First Amendment generally protects speech (or written communication), rather than conduct, and “[s]peech in aid of pharmaceutical marketing” is no exception.<sup>171</sup> Most courts considering “the constitutionality of various FDA labeling, advertising and promotion regulations and/or disclosure requirements have proceeded directly to a commercial speech analysis,” applying a less exacting standard of review than the strict scrutiny usually afforded First Amendment protected speech.<sup>172</sup> The assumption that all off-label “promotion” is inherently commercial speech may be consistent with the belief that there is a “common-sense distinction between speech proposing a commercial transaction, which occurs in an area traditionally subject to government regulation, and other varieties of speech.”<sup>173</sup> The speech and conduct of pharmaceutical companies have been subject to government regulation for nearly eighty years,<sup>174</sup> which might suggest that all communications used by pharmaceutical companies for purposes of increasing market share or sales of their products are inherently commercial in nature.

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169. 447 U.S. 557 (1980).

170. Cortez, *supra* note 48, at 414 (“A notable observation from reviewing the FDA-related cases is that courts sometimes examine the scope and purposes of the law being challenged to determine whether the speech it regulates is commercial or not. This approach conflates the first-order question of whether the speech is commercial (*Bolger*) with the second-order question of whether the restriction violates free speech rights (*Central Hudson*).”).

171. Sorrell v. IMS Health Inc., 131 S. Ct. 2653, 2659 (2011) (declaring a state statute, which deprived pharmaceutical and data mining companies of data that could help pharmaceutical companies create better sales messages, unconstitutional).

172. E.g., *Wash. Legal Found.*, 13 F. Supp. at 61; *see also* Pearson v. Shalala, 14 F. Supp. 2d 10, 21 (D.D.C. 1998) (using the commercial speech framework to uphold FDA regulations), *rev’d*, 164 F.3d 650 (D.C. Cir. 1999); *Nutritional Health All. v. Shalala*, 953 F. Supp. 526 (S.D.N.Y. 1997) (applying the *Central Hudson* framework and finding a law regulating health labels unconstitutionally overbroad); *Nat’l Council for Improved Health v. Shalala*, 893 F. Supp. 1512, 1516–17 (D. Utah 1995) (noting that a facial challenge to the labeling regulations implicated the First Amendment, and employing the *Central Hudson* framework to determine if the regulations infringed free speech); *United States v. Gen. Nutrition, Inc.*, 638 F. Supp. 556, 562 (W.D.N.Y. 1986) (declaring labeling as “clearly commercial speech”).

173. *Bolger v. Youngs Drug Prods. Corp.*, 463 U.S. 60, 64 (1983) (quoting *Ohralik v. Ohio State Bar Ass’n*, 436 U.S. 447, 455–56 (1978)).

174. HUTT ET AL., *supra* note 23, at 5 (“A single statute, the 1938 FD&C Act, as amended, provides the basic legal framework controlling the activities of producers of food, drugs, cosmetics, medical devices, and tobacco products.”).

Even so, the Supreme Court has been hesitant to draw a bright line between publicly “important” or “interesting” commercial speech and commercial speech of no public value.<sup>175</sup> Indeed, when asked to apply lesser scrutiny to the speech of a labor union president because he was “engaged in business activities” and received compensation for doing so, the Court found the attempted distinction between “economic activity” and rigorously protected “liberties of the citizen” to be “at once too simple, too general, and too inaccurate to be determinative.”<sup>176</sup> The Court has noted on multiple occasions that advertising may both propose a commercial transaction and contain “factual material of clear ‘public interest,’”<sup>177</sup> and “that speech is not rendered commercial by the mere fact that it relates to an advertisement.”<sup>178</sup> Additionally, speech that is “in the abstract . . . ‘merely commercial’” may not “retain[] its commercial character when it is inextricably intertwined with otherwise fully protected speech.”<sup>179</sup> “Where the line shall be placed in a particular application rests, not on such generalities, but on the concrete clash of particular interests and the community’s relative evaluation both of them and of how the one will be affected by the specific restriction, the other by its absence.”<sup>180</sup>

The “particular interests” at play in the government’s efforts to limit the dissemination of truthful off-label information are multifaceted. They include not only government employees’ sincere interest in protecting public health and pharmaceutical company shareholders’ interest in return on their financial investment, but also many government officials’ interests in political or professional advancement, pharmaceutical company employees’ interests in getting the right drugs to the right patients, prescribers’ interests in providing quality care for their patients, and patients’ interests in improved quality and quantity of life; and all of these people are critically interested in providing for themselves and those who depend upon them, including their kin, kith, employees, supervisors, and colleagues. The exchange of information, goods, and services abounds within

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175. See *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 636 (1985) (“More subject to doubt, perhaps, are the precise bounds of the category of expression that may be termed commercial speech, but it is clear enough that the speech at issue in this case—advertising pure and simple—falls within those bounds.”); *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 765 (1976) (“Moreover, there is another consideration that suggests that no line between publicly ‘interesting’ or ‘important’ commercial advertising and the opposite kind could ever be drawn.”). *But see id.* at 771 n.24 (“In concluding that commercial speech enjoys First Amendment protection, we have not held that it is wholly undifferentiable from other forms. There are commonsense differences between speech that does ‘no more than propose a commercial transaction’ and other varieties.” (quoting *Pittsburgh Press Co. v. Pittsburgh Comm’n on Human Relations*, 413 U.S. 376, 385 (1972))).

176. *Thomas v. Collins*, 323 U.S. 516, 531 (1945).

177. *E.g.*, *Va. Citizens Consumer Council, Inc.*, 425 U.S. at 760 (quoting *Bigelow v. Virginia*, 421 U.S. 809, 822 (1975) (concluding that a newspaper publication announcing the availability of abortions in New York not only proposed a commercial transaction, but also contained information of clear public interest)).

178. *E.g.*, *Pittsburgh Press Co.*, 413 U.S. at 384.

179. *Riley v. Nat’l Fed’n of the Blind of N.C., Inc.*, 487 U.S. 781, 796 (1988) (applying strict scrutiny to a state statute regulating charitable solicitation by professional fundraisers upon finding that such commercial speech was inextricably intertwined with informative and persuasive speech).

180. *Thomas*, 323 U.S. at 531.

these many relationships and runs the gamut from purely commercial to entirely noncommercial (whether scientific, educational, political, professional, or personal).

The bulk of information on off-label uses of drugs inherently flows *from* pharmaceutical companies (the entities that know the drugs best),<sup>181</sup> to the government, prescribers, and patients. Because of the fiduciary duties that for-profit corporations have to their shareholders, communication of this information is broadly characterized as “promotion” and, as such, “commercial” regardless of context. This broad characterization, though, is inconsistent with the FDA’s own recognition of both promotional and nonpromotional communication between pharmaceutical companies and prescribers.<sup>182</sup> Similarly, this broad characterization is inconsistent with Supreme Court decisions that have recognized that not all communication created out of a financial incentive is appropriately considered commercial,<sup>183</sup> and that corporations can communicate information and opinions beyond the merely commercial.<sup>184</sup>

Information on off-label uses of prescription drugs is used to inform decision-making separate and apart from the mere purchase of the products by government officials, payers, pharmacists, prescribers, and patients alike.<sup>185</sup> Accord-

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181. See HUTT ET AL., *supra* note 23, at 925 (“Doctors prescribing drugs off-label sometimes need information from the manufacturer—the entity that knows the drug best—about how to do so safely [sic] and effectively.”).

182. See FDA, DISTRIBUTING SCIENTIFIC AND MEDICAL PUBLICATIONS ON UNAPPROVED NEW USES, *supra* note 14, at 7–8 (“[Reprints of] the scientific or medical journal article distributed by a manufacturer *should* . . . [b]e distributed separately from the delivery of information that is promotional in nature. For example, if a sales representative delivers a reprint to a physician in his or her office, the reprint should not be attached to any promotional material the sales representative uses or delivers during the office visit. To the extent that the recipients of the scientific or medical journal article have questions, the sales representative should refer the questions to a medical/scientific officer or department, and the officer or department to which the referral is made should be independent of the sales and/or marketing departments. Similarly, while reprints may be distributed at medical or scientific conferences in settings appropriate for scientific exchange, reprints should not be distributed in promotional exhibit halls or during promotional speakers’ programs.”).

183. See, e.g., *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 760 (1976); *Bigelow v. Virginia*, 421 U.S. 809, 822 (1975).

184. See *Citizens United v. Fed. Election Comm’n*, 558 U.S. 310, 342–43 (2010) (noting that political speech does not lose its First Amendment protection merely because it is put forth by a corporation); *Pac. Gas & Elec. Co. v. Public Util. Comm’n of Cal.*, 475 U.S. 1, 8 (1986) (plurality opinion) (“The identity of the speaker is not decisive in determining whether speech is protected. Corporations and other associations, like individuals, contribute to the ‘discussion, debate, and the dissemination of information and ideas’ that the First Amendment seeks to foster.” (quoting *First Nat’l Bank of Boston v. Bellotti*, 435 U.S. 765, 783 (1978))); *First Nat’l Bank of Boston*, 435 U.S. at 784 (1978) (“We thus find no support in the First or Fourteenth Amendment, or in the decisions of this Court, for the proposition that speech that otherwise would be within the protection of the First Amendment loses that protection simply because its source is a corporation that cannot prove, to the satisfaction of a court, a material effect on its business or property.”).

185. See Eleanor M. Peretto et al., *Communication About Results of Comparative Effectiveness Studies: A Pharmaceutical Industry View*, 31 HEALTH AFFAIRS 2213, 2214 (2012) (“Drug effectiveness under real-world conditions is of major interest to patients, clinicians, and payers. But the studies that provide this information often use observational designs, as opposed to randomized controlled trials, and they often assess outcomes that are not necessarily included on the label.”).

ingly, it seems likely that many forms of off-label “promotion,” whether in the form of correcting a misunderstanding expressed in a public forum<sup>186</sup> or reporting the progress of ongoing clinical trials, are not inherently or entirely commercial in nature.

Much of the information on off-label uses is part of the larger universe of scientific speech, which generally receives strict scrutiny protection like political speech.<sup>187</sup> As with the information contained in political speech, which government officials use to craft and revise legislation, regulations, and policies, pharmaceutical companies use the information (generated by both their own research and their competitors’ research) to evaluate current research efforts as well as identify and prioritize possible future research and development. These broader-based analytical decisions are well informed by scientific research and speech designed to inform general knowledge.

Science, however, cannot always easily be translated into terms specific to treating individuals. Science informs general knowledge, whereas clinical care requires focus on the specific individuals who may or may not be representative of a larger patient population.<sup>188</sup> Prescribers may seek and use information beyond pure scientific speech to inform their prescribing practices.<sup>189</sup> Additionally, the necessity and immediacy of treating an individual does not always align with

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186. FDA, RESPONDING TO UNSOLICITED REQUESTS, *supra* note 57, at 3 (“FDA recognizes that [pharmaceutical companies] are capable of responding to requests about their own named products in a truthful, non-misleading, and accurate manner. Furthermore, as these firms are regulated by FDA and have robust and current information about their products, FDA recognizes that it can be in the best interest of public health for a firm to respond to unsolicited requests for information about off-label uses of the firm’s products that are addressed to a public forum, as other participants in the forum who offer responses may not provide or have access to the most accurate and up-to-date information about the firm’s products.”).

187. *E.g.*, Bd. of Trs. of Leland Stanford Junior Univ. v. Sullivan, 773 F. Supp. 472, 474 (D.D.C. 1991) (“[T]he First Amendment protects scientific expression and debate just as it protects political and artistic expression.”).

188. See generally Jennifer L. Herbst, *How Medicare Part D, Medicaid, Electronic Prescribing, and ICD-10 Could Improve Public Health (But Only If CMS Lets Them)*, 24 HEALTH MATRIX 209, 219 (2014) (discussing the importance of individual patient considerations in the practice of medicine).

189. The World Health Organization (WHO) and STEPS framework, adopted by the American Academy of Family Physicians, both recommend prescribers consider pricing when choosing drugs to prescribe. T. P. G. M. DE VRIES ET AL., WORLD HEALTH ORG., GUIDE TO GOOD PRESCRIBING: A PRACTICE MANUAL 32 (1994), [http://whqlibdoc.who.int/hq/1994/WHO\\_DAP\\_94.11.pdf](http://whqlibdoc.who.int/hq/1994/WHO_DAP_94.11.pdf); Madelyn Pollock, Oralia V. Bazaldua & Alison E. Dobbie, *Appropriate Prescribing of Medications: An Eight-Step Approach*, 75 AM. FAMILY PHYSICIAN 231, 232–33 (2007). In addition, the WHO also suggests prescribers consider a drug’s “suitability,” which would include consideration of the ease of administration (e.g., liquid form for children or elderly patients, one or more doses needed daily); or other conditions (such as pregnancy) or illnesses that might affect a patient’s ability to take the drug; or the likelihood that the clinical trial subjects were representative of the patients seen by a particular physician. G. M. DE VRIES ET AL., *supra*, at 31–32. Similarly, the STEPS framework recommends that prescribers consider a drug’s “simplicity,” including whether it “can be taken less often, does not require special handling (e.g., refrigeration), or does not interact with other commonly used drugs.” Allen F. Shaughnessy, *STEPS Drug Updates*, 68 AM. FAMILY PHYSICIAN 2342, 2342 (2003).

the more time-consuming and resource-dependent demands of clinical trials.<sup>190</sup> Most important, though, for purposes of this Article is that prescribers, qua prescribers, are factually, ethically, and legally set apart from consumers of prescription drugs (i.e., those to whom a commercial transaction might be proposed).

Factually, most prescribers do not, and many may not, directly purchase the prescription drugs promoted by pharmaceutical companies for their patients.<sup>191</sup> While the pharmaceutical company representatives deemed “promotional” by the government are often part of a “sales” department of the company<sup>192</sup> and many have bonuses based upon their “sales,”<sup>193</sup> it is not the physician or other prescriber purchasing these drugs for the vast majority of prescription drugs.<sup>194</sup> Despite the tendency to characterize prescribers as such, the conversation between the pharmaceutical company employee and prescriber is most often not one with a potential customer.<sup>195</sup> Indeed, the “primary duty” of pharmaceutical “sales” representatives “is to obtain nonbinding commitments from physicians to prescribe their employer’s prescription drugs in appropriate cases.”<sup>196</sup> A minority of physicians choose to dispense prescription drugs directly to patients,<sup>197</sup> but most do not.<sup>198</sup>

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190. See Amitabh Chandra, Dhruv Khullar & Thomas H. Lee, *Addressing the Challenge of Gray-Zone Medicine*, 372 NEW ENG. J. MED. 203–04 (2015).

191. The practice of physician dispensing, as distinguished from the administration of drugs, is disproportionately concentrated in physician practices treating injured workers. Meier, *supra* note 55, at B1 (“Over the last two years, states nationwide have moved to crack down on so-called physician dispensing of prescription drugs, a practice largely limited to doctors who treat injured workers.”); see also *Christopher v. SmithKline Beecham Corp.*, 132 S. Ct. 2156, 2173 (2012) (“[P]hysician-administered drugs, such as vaccines and other injectable pharmaceuticals, that are also ordered by the physician directly rather than purchased by the end user at a pharmacy with a prescription from the physician.”).

192. *Christopher*, 132 S. Ct. at 2161 (explaining that pharmaceutical sales representative were appropriately considered “outside salesmen” for purposes of the Fair Labor Standards Act (FLSA), despite the fact that their “primary duty [was] to obtain nonbinding commitments from physicians to prescribe their employer’s prescription drugs in appropriate cases”).

193. See *United States v. Caronia*, 703 F.3d 149, 155–56 (2d Cir. 2012) (“In March 2005, Orphan hired Caronia as a Specialty Sales Consultant to promote Xyrem. Caronia primarily worked in Queens, Nassau, and Suffolk counties. Caronia’s salary was based on his individual sales.”).

194. The Court’s decision to characterize detailers as “outside salesmen” for purposes of the FLSA in *Christopher v. SmithKline Beecham Corp.* was based primarily on the fact that the statutory definition of “sale” was more expansive than the term’s ordinary meaning. *Christopher*, 132 S. Ct. at 2171 (2012) (“Congress defined ‘sale’ to include both the unmodified word ‘sale’ and transactions that might not be considered sales in a technical sense, including exchanges and consignments for sale.”). In his dissent, Justice Breyer, joined by Justices Ginsburg, Sotomayor and Kagan, provided a step-by-step explanation for why detailers do not “sell” prescription drugs to prescribers. *Id.* at 2176–77 (Breyer, J., dissenting).

195. See, e.g., *Caronia*, 703 F.3d at 156 (“Caronia and Gleason were audio-recorded on two occasions as they promoted Xyrem for unapproved uses, including unapproved indications and unapproved subpopulations. The first conversation was recorded on October 26, 2005 between Caronia and Dr. Stephen Charno, a physician who, as a government cooperator, posed as a prospective Xyrem customer.” (emphasis added)).

196. *Christopher*, 132 S. Ct. at 2161.

197. “There’s a bit of a trend in the last few years for more and more doctors to dispense medications directly to patients rather than send them to their pharmacist with prescriptions in hand.” Mi-

Additionally, the mere fact that a prescriber writes a valid prescription does not inherently mean that the particular drug will be purchased, whether due to a patient's decision to leave the prescription unfilled<sup>199</sup> or a third-party payer's coverage determination for a particular product.<sup>200</sup> Indeed, it is this disconnect

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chael Cohen, *When Doctors—Not Pharmacists—Dispense Meds*, PHILA. INQUIRER (Oct. 17, 2013, 5:02 PM), <http://www.philly.com/philly/health/Do-consumers-benefit-when-doctors-dispense-medications-instead-of-pharmacists-.html#eYjEWLclshQ9x2xG.99>. Some healthcare providers may choose to dispense drugs personally as an attempt to increase patient adherence to and physician monitoring of prescribed treatments. Meier, *supra* note 55, at B1 (“Doctors say the practice benefits patients because it is convenient and allows physicians to better monitor the patient’s use of medication . . .”); Debra Hughes, *Should You Sell Drugs To Patients?*, MEDSCAPE BUS. MED. (May 9, 2013), <http://www.medscape.com/viewarticle/803653> (“[P]hysicians and staff derive satisfaction from seeing patients adhere to their medication regimens . . .”). Others do it to reduce writing and dispensing errors. See DOCTORS DISPENSING DRUGS, <http://doctorsdispensingdrugs.com/doctorsdispensingdrugs/Welcomed.html> (last visited Nov. 1, 2015) (“Physician dispensing increases compliance rate of patients and eliminates writing and dispensing errors.”). Others, still, do so to increase revenue for their practice. Cohen, *supra* (“Doctors see dispensing as a way to offset declining reimbursements by creating an ancillary revenue source.”); see also Barry Meier & Katie Thomas, *Drugs Dispensed by Doctors Cost Insurers Dearly*, N.Y. TIMES, July 12, 2012, at A1 (“Doctors can make tens of thousands of dollars a year operating their own in-office pharmacies. The practice has become so profitable that private equity firms are buying stakes in the businesses, and political lobbying over the issue is fierce.”); Ronald Sullivan, *Number of Doctors Selling Prescription Drugs Grows*, N.Y. TIMES, Mar. 19, 1987, at B1 (“State medical societies such as the one in New York said doctors could increase their incomes by as much as \$10,000 to \$40,000 a year by selling the drugs they prescribe at a time when economic competition among doctors and hospitals is sharply increasing. The groups also said the practice offered patients, particularly the elderly, a way to save a trip to the drugstore.”); Richard Reece, *Why Doctors Should Profit from Dispensing Medications*, KEVINMD.COM (Jan. 15, 2011), <http://www.kevinmd.com/blog/2011/01/doctors-profit-dispensing-medications.html> (“[M]aybe doctors should profit from dispensing medications from their office to offset declining reimbursements and rising expenses by using prescriptions as a source of ancillary revenues.”); DOCTORS DISPENSING DRUGS, *supra* (contending that point-of-care dispensing “[c]reates new, easy to generate, high margin revenue stream” for healthcare providers).

198. Francesca Lunzer Kritz, *Doctor? Or Druggist?*, WASH. POST (Oct. 30, 2007), <http://www.washingtonpost.com/wp-dyn/content/article/2007/10/26/AR2007102602484.html> (“Less than 10 percent of U.S. physicians sell prescription medications to their patients, according to the journal *Physicians Practice*. But Mark Bard, president of Manhattan Research, a health-care market research firm in New York, says that figure could reach 25 percent in the next five to 10 years.”).

199. See Tamblin et al., *supra* note 165, at 441 (stating that 31.3% of more than 37,000 prescriptions for nearly 16,000 primary care patients were not purchased).

200. See Jonathan D. Rockoff, *As Doctors Lose Clout, Drug Firms Redirect the Sales Call*, WALL ST. J. (Sept. 24, 2014, 10:30 PM), <http://www.wsj.com/articles/as-doctors-lose-clout-drug-firms-redirect-the-sales-call-1411612207> (“Kendall French used to pitch drugs to doctors who could prescribe them. But many of those doctors now work for hospitals that don’t give them final say over what is on the menu of medicines they can pick.”); see also Beth Battagliano, Op-Ed., *CT Insurers Force Women to Use Medications Off-Label to Treat Hot Flashes*, CT MIRROR (Feb. 6, 2015), <http://ctmirror.org/2015/02/06/op-ed-ct-insurers-force-women-to-use-medications-off-label-to-treat-hot-flashes/> (“Forced off-label prescribing occurs when insurers require patients to try and fail on prescription medicines that are not approved by the Food and Drug Administration (FDA) for the treatment of their medical condition—before granting access to those that are. Insurers require this extra step not because the off-label treatment is better, but because it is cheaper.”). In truth, physicians have not been able to make the final decision for prescription drugs since HMOs started using utilization review as a way to manage costs. See Michael R. Pollard, *Managed Care and a Changing Pharmaceutical Industry*, 9 HEALTH AFFAIRS 55, 57 (1990) (“[T]ried and true marketing efforts targeted on indi-

tion between prescription and sale that leads to many of the administrative frustrations experienced by prescribers and patients alike.<sup>201</sup>

Ethically, unlike most business people (including most consumers), prescribers are required by their professions to put their patients' best interests before any personal financial interest when prescribing treatment.<sup>202</sup> This "ethical necessity" takes precedence over any possible sale.<sup>203</sup>

Legally, the authority to prescribe is governed by state law,<sup>204</sup> and has been granted to a select group of licensed professionals in each state, including physicians, dentists, advanced practice registered nurses, physician assistants, psychologists, podiatrists, and optometrists.<sup>205</sup> Prescription drugs are, in turn, drugs that "shall be dispensed only (i) upon a written prescription of a practitioner licensed by law to administer such drug."<sup>206</sup> In order to dispense a prescription drug, one must first purchase it from the wholesaler or distributor<sup>207</sup> and then

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vidual physicians are becoming less effective in moving products because physicians often do not make the ultimate decisions in selecting drugs.").

201. See Danielle Ofri, Op-Ed., *Adventures in 'Prior Authorization,'* N.Y. TIMES, Aug. 4, 2014, at A21 (discussing clinical frustrations in navigating "prior authorization" procedures after spending years honing treatment regimen for individual patient who had recently switched insurance companies).

202. See Barak Richman, *On Doctors and Judges*, 58 DUKE L.J. 1731, 1732 (2009) ("Unlike most businesspeople, physicians are expected to prescribe advice and treatment that are divorced from their pecuniary interests . . ."); *Opinion 8.06—Prescribing and Dispensing Drugs and Devices*, AM. MED. ASS'N, <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion806.page> (last visited Nov. 1, 2015) ("Physicians may dispense drugs within their office practices provided such dispensing primarily benefits the patient."); see, e.g., AM. NURSES ASS'N, CODE OF ETHICS FOR NURSES WITH INTERPRETIVE STATEMENTS Provision 2.2 (2015), <http://www.nursingworld.org/provision-2> ("Nurses must examine the conflicts arising between their own personal and professional values, the values and interests of others who are also responsible for patient care and healthcare decisions, as well as those of patients. Nurses strive to resolve such conflicts in ways that ensure patient safety, guard the patient's best interests and preserve the professional integrity of the nurse.").

203. *Christopher v. SmithKline Beecham Corp.*, 132 S. Ct. 2156, 2179 (2012) (Breyer, J., dissenting) ("Given the fact that the doctor buys nothing, the fact that the detailer sells nothing to the doctor, and the fact that any 'nonbinding commitment' by the doctor must, of *ethical necessity*, be of secondary importance, there is nothing about the detailer's visit with the doctor that makes the visit (or what occurs during the visit) 'tantamount . . . to a paradigmatic sale.'" (omission in original) (emphasis added)).

204. See, e.g., *United States v. Shock*, 379 F.2d 29, 32–33 (8th Cir. 1967).

205. HUTT ET AL., *supra* note 23, at 807–08.

206. 21 U.S.C.A. § 353(b)(1)(B)(i) (West 2015). The other circumstances in which prescription drugs can be lawfully dispensed are

(ii) upon an oral prescription of such practitioner which is reduced promptly to writing and filed by the pharmacist, or (iii) by refilling any such written or oral prescription if such refilling is authorized by the prescriber either in the original prescription or by oral order which is reduced promptly to writing and filed by the pharmacist.

*Id.* § 353(b)(1)(B)(ii)–(iii).

207. *Id.* § 360eee-1(d)(3) ("[T]he trading partners of a dispenser may be only authorized trading partners."); *id.* § 360eee(2) (defining "authorized" as one with a "valid registration" or license); *id.* 360eee(23)(A)–(B) (defining "trading partner" as "a manufacturer, repackager, wholesale distributor,

sell or administer it to a patient, but only after a valid prescription has been issued by a licensed professional. Prescribing is legally distinct from dispensing.<sup>208</sup>

Unlike prescribing, dispensing inherently involves a commercial transaction—a specific product changes possession in exchange for money. The authority to dispense prescription drugs is governed both by federal law<sup>209</sup> and by the states.<sup>210</sup> Some states allow physicians<sup>211</sup> and nurses<sup>212</sup> to dispense prescription drugs, while other states explicitly limit dispensing of drugs to pharmacists.<sup>213</sup> Consumers of prescription drugs, by contrast, need not have any requisite education, training, experience, or other professional vetting.

Any person authorized by law to dispense or administer prescription drugs is considered a “dispenser” for purposes of the recently enacted Drug Quality and Security Act (DQSA).<sup>214</sup>

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dispenser” or third party logistics provider from whom one accepts direct possession or ownership of a product).

208. *Id.* § 353(b)(1) (describing the process in which dispensing of a drug is contingent upon a prescription from a licensed practitioner, and therefore differentiating the two actions).

209. *Id.* § 360eee(3)(A) (stating that a “dispenser” can be “a retail pharmacy, hospital pharmacy, a group of chain pharmacies under common ownership and control that do not act as a wholesale distributor, or any other person authorized by law to dispense or administer prescription drugs, and the affiliated warehouses or distribution centers of such entities under common ownership and control that do not act as a wholesale distributor”).

210. *See id.* § 360eee(2)(D) (defining an authorized dispenser as one “having a valid license under State law”).

211. *E.g.*, ARIZ. REV. STAT. ANN. § 32-1491(A) (2015) (“A doctor of medicine may dispense drugs and devices kept by the doctor . . .”); 225 ILL. COMP. STAT. ANN. 60/33(a) (West 2015) (“Any person licensed under this Act to practice medicine in all of its branches shall be authorized to purchase legend drugs requiring an order of a person authorized to prescribe drugs, and to dispense such legend drugs in the regular course of practicing medicine.”); IOWA CODE ANN. § 147.107(1) (West 2015) (“A person, other than a pharmacist, physician, dentist, podiatric physician, or veterinarian who dispenses as an incident to the practice of the practitioner’s profession, shall not dispense prescription drugs or controlled substances.”); MICH. COMP. LAWS ANN. § 333.17703(3) (West 2015) (“Dispensing prescriber” means a prescriber, other than a veterinarian, who dispenses prescription drugs.”); MO. ANN. STAT. § 334.106(1) (West 2015) (“[A] physician may prescribe, administer or dispense controlled substances for a therapeutic purpose to a person diagnosed and treated by a physician for a condition resulting in intractable pain . . .”); OR. REV. STAT. ANN. § 677.089(1) (West 2015) (“Prescription drugs dispensed by a physician shall be personally dispensed by the physician.”).

212. *E.g.*, CAL. BUS. & PROF. CODE § 2725.1(a) (West 2015) (“Notwithstanding any other provision of law, a registered nurse may dispense drugs or devices upon an order by a licensed physician and surgeon or an order by a certified nurse-midwife, nurse practitioner, or physician assistant . . . if the registered nurse is functioning within a licensed primary care clinic . . .”); MD. CODE ANN., HEALTH OCC. § 8-508(b) (West 2105) (“A nurse practitioner may personally prepare and dispense a starter dosage of any drug the nurse practitioner is authorized to prescribe to a patient . . .”); OR. REV. STAT. ANN. § 678.390(2) (West 2015) (“A certified nurse practitioner or certified clinical nurse specialist may submit an application to the Oregon State Board of Nursing to dispense prescription drugs.”).

213. *E.g.*, MONT. CODE ANN. § 37-2-104(1) (West 2015) (“Except as otherwise provided by this section, it is unlawful for a medical practitioner to engage, directly or indirectly, in the dispensing of drugs.”).

214. Drug Quality and Security Act, Pub. L. No. 113-54, § 202, 127 Stat. 587, 599 (2013).

[The DQSA] facilitates the tracing of products through the pharmaceutical distribution supply chain by requiring . . . manufacturers, repackagers, wholesale distributors, and dispensers . . . to exchange transaction information, transaction history, and a transaction statement (product tracing information) when engaging in [commercial] transactions involving certain prescription drugs.<sup>215</sup>

As of July 1, 2015, dispensers of prescription drugs are now required to maintain records of a product’s “transaction history,” “transaction information,” and a “transaction statement.”<sup>216</sup> Although many of the current prescribers purchasing prescription drugs will likely be exempted from personally providing product-tracing information,<sup>217</sup> the previous owners of the prescription drug products (whether the manufacturers, wholesale distributors, or repackagers) will also be tracking sales of the products.<sup>218</sup>

Pharmaceutical manufacturers have an undeniable commercial relationship with the dispensers of prescription drugs. Their conversations and communications with prescribers, however, are not always or inherently commercial in nature because the act of prescribing is not, in itself, a commercial transaction; the speech does not discuss, encourage, or inform the possible exchange of goods or services between the two parties to the communication. As such, speech uttered and heard solely to inform prescribing decisions cannot “propose a commercial transaction”<sup>219</sup> as is required in order to be considered commercial speech for First Amendment analysis.

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215. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: DSCSA STANDARDS FOR THE INTEROPERABLE EXCHANGE OF INFORMATION FOR TRACING OF CERTAIN HUMAN, FINISHED, PRESCRIPTION DRUGS: HOW TO EXCHANGE PRODUCT TRACING INFORMATION 1 (2014), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm424895.pdf> [hereinafter FDA, DSCSA STANDARDS]; see also 21 U.S.C.A. § 360eee(26)(J) (“[T]ransaction information’ means . . . the business name and address of the person to whom ownership is being transferred . . .”); *id.* § 360eee(25) (“The term ‘transaction history’ means a statement in paper or electronic form, including the transaction information for each prior transaction going back to the manufacturer of the product.”); *id.* § 360eee(27)(B) (“The ‘transaction statement’ is a statement . . . that the entity transferring ownership in a transaction . . . received the product from a person that is authorized as required under the Drug Supply Chain Security Act . . .”).

216. 21 U.S.C.A. § 360eee-1(d)(1)(A)(iii).

217. *Id.* § 360eee-1(d)(5) (explaining that dispenser record requirements “shall not apply to licensed health care practitioners authorized to prescribe or administer medication under State law or other licensed individuals under the supervision or direction of such practitioners who dispense or administer product in the usual course of professional practice”).

218. *Id.* § 360eee-1(d)(1)(A)(i) (explaining that dispensers are only allowed to accept ownership of a product if the “previous owner . . . provides transaction history, transaction information, and a transaction statement”). The FDA has, however, provided an extension to manufacturers, wholesale distributors, and repackagers, which may delay full-scale implementation of the product tracing system. See FDA, DSCSA STANDARDS, *supra* note 215, at 1.

219. *United States v. United Foods, Inc.*, 533 U.S. 405, 409 (2001) (citing *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 762 (1976)).

V. DISCUSSION AND DISSEMINATION OF OFF-LABEL INFORMATION DOES MORE THAN MERELY PROPOSE A COMMERCIAL TRANSACTION.

Pharmaceutical companies' dissemination and discussion of off-label information is driven largely by the financial interests of the corporations' shareholders, management, and employees. Even so, "[i]t is not clear that a professional's speech is necessarily commercial whenever it relates to that person's financial motivation for speaking."<sup>220</sup> Likewise, even if all prescribers are potential end consumers<sup>221</sup> (despite the overwhelming majority who do not dispense drugs),<sup>222</sup> their consumer status does not settle the question of whether discussion of off-label information is merely commercial in nature. In some situations, commercial speech is "inextricably intertwined" with the flow of fully protected information or advocacy that, in the absence of the commercial solicitation, would cease.<sup>223</sup> In these situations, speech that is commercial in nature receives full First Amendment protection because of the social value of the noncommercial content.

In prior cases, fully protected "hybrid" speech that combined both financially driven and noncommercial "component parts" included communications by professional fundraisers soliciting contributions for charitable organizations,<sup>224</sup> paid individuals circulating a petition for state deregulation of the trucking industry,<sup>225</sup> and salaried, full-time labor union organizers soliciting membership for their labor unions.<sup>226</sup> In each of these cases, the Court decided that the hybrid nature of the speech warranted strict scrutiny of the government's attempts to regulate it despite the speakers' financial interests.<sup>227</sup> In each of these cases, the

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220. *Riley v. Nat'l Fed'n of the Blind of N.C., Inc.*, 487 U.S. 781, 795 (1988).

221. *Cortez*, *supra* note 48, at 406 ("[P]hysicians and other prescribers that properly belong to the medical and scientific community are also potential customers.")

222. *See* *Kritz*, *supra* note 198 ("Less than 10 percent of U.S. physicians sell prescription medications to their patients, according to the journal *Physicians Practice*.")

223. *Riley*, 487 U.S. at 796 (citing *Vill. of Schaumburg v. Citizens for a Better Env't*, 444 U.S. 620, 632 (1980)).

224. *E.g., id.*; *Sec'y of State of Md. v. Joseph H. Munson Co.*, 467 U.S. 947, 950 (1984); *Schaumburg*, 444 U.S. at 620-21 (1980).

225. *Meyer v. Grant*, 486 U.S. 414, 422 n.5 (1988).

226. *Thomas v. Collins*, 323 U.S. 516 (1945).

227. *Riley*, 487 U.S. at 796 ("Regulation of a solicitation 'must be undertaken with due regard for the reality that solicitation is characteristically intertwined with informative and perhaps persuasive speech' . . . . Thus, where, as here, the component parts of a single speech are inextricably intertwined, we cannot parcel out the speech, applying one test to one phrase and another test to another phrase. Such an endeavor would be both artificial and impractical. Therefore, we apply our test for fully protected expression." (emphasis added) (quoting *Schaumburg*, 444 U.S. at 632)); *see also Meyer*, 486 U.S. at 424-25 (providing that the financial interests of paid advocates for political change did not result in lesser First Amendment protection of one-on-one communication of political speech); *Schaumburg*, 444 U.S. at 635 (holding that the speech of paid solicitors who combined "the solicitation of financial support with the 'functions of information dissemination, discussion, and advocacy of public issues'" was fully protected noncommercial speech (quoting *Citizens for a Better Env't v. Vill. of Schaumburg*, 590 F.2d 220, 225 (7th Cir. 1978))); *Thomas*, 323 U.S. at 533-38 (providing that fully-protected speech on the advantages of workers' organization was "inseparable" from invitations to join union extended by the paid president of the International Union U.A.W.).

listeners did not fit the typical profile of a consumer. Rather, in *Riley v. National Federation of the Blind of N.C., Inc.*,<sup>228</sup> *Secretary of State of Maryland v. Joseph H. Munson Co.*,<sup>229</sup> and *Village of Schaumburg v. Citizens for a Better Environment*,<sup>230</sup> the listeners were potential donors for charitable organizations. In *Meyer v. Grant*,<sup>231</sup> the listeners were possible petition signatories.<sup>232</sup> In *Thomas v. Collins*,<sup>233</sup> the listeners were potential union members.<sup>234</sup> In all of these cases, the listeners were also potentially learning information of public interest critical to informing their civic engagement and their votes.

“Purely factual matter of public interest may claim protection.”<sup>235</sup> Similarly, the “exposition of ideas,”<sup>236</sup> which advances “truth, science, morality, and arts in general” and “diffuse[es] . . . liberal sentiments on the administration of Government,”<sup>237</sup> are protected as noncommercial speech. Of course, a smattering of political, scientific, educational, or religious speech does not inherently render speech noncommercial, especially where the listeners are typical potential consumers and the information is unlikely to affect decisions beyond those of an individual’s “home economics.”<sup>238</sup> Instead, the commercial and noncommercial aspects must be “inextricably intertwined,”<sup>239</sup> “inseparable.”<sup>240</sup> The Court considered Tupperware parties that consisted of both demonstrating and offering products for sale to groups of prospective buyers to be commercial speech despite the inclusion of “home economics” elements in the demonstration.<sup>241</sup> After all, “[n]o law of man or of nature makes it impossible to sell housewares without teaching home economics, or to teach home economics without selling housewares.”<sup>242</sup>

Unlike the sale of housewares, the sale of prescription drugs requires the education of prescribers, “learned intermediaries” without which our prescription drug system would not function. Prescription drugs are unavoidably unsafe

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228. 487 U.S. 781 (1988).

229. 467 U.S. 947 (1984).

230. 444 U.S. 620 (1980).

231. 486 U.S. 414 (1988).

232. See *Meyer*, 486 U.S. at 417.

233. 323 U.S. 516 (1945).

234. See *Thomas*, 323 U.S. at 518.

235. *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 762 (1976) (citing *Bigelow v. Virginia*, 421 U.S. 809, 822 (1975); and *Thornhill v. Alabama*, 310 U.S. 88, 102 (1940)).

236. *Chaplinsky v. New Hampshire*, 315 U.S. 568, 572 (1942).

237. *Roth v. United States*, 354 U.S. 476, 484 (1957) (quoting 1 JOURNALS OF THE CONTINENTAL CONGRESS 108 (1774)).

238. *Bd. of Trs. of State Univ. of N.Y. v. Fox*, 492 U.S. 469, 474–75 (1989).

239. *Riley v. Nat’l Fed’n of the Blind of N.C., Inc.*, 487 U.S. 781, 796 (1988) (citing *Vill. of Schaumburg v. Citizens for a Better Env’t*, 444 U.S. 620, 632 (1980)).

240. *Thomas v. Collins*, 323 U.S. 516, 534 (1945).

241. *Fox*, 492 U.S. at 474.

242. *Id.*

products<sup>243</sup> with proven therapeutic value for a subpopulation of patients. The drugs are too complicated, too nuanced for laypeople to purchase directly,<sup>244</sup> but simultaneously too valuable, both for an individual's health and the public health at large, to ban them outright. Instead, unlike the vast majority of goods and services for sale, we require multiple licensed professionals to serve as gatekeepers to the products. As a result, "[c]ourts have concluded that as long as a drug . . . provides net benefits to some persons under some circumstances, *the drug . . . manufacturer should be required to instruct and warn health-care providers of the foreseeable risks and benefits.*"<sup>245</sup> Accordingly, detailers have a duty (arguably, their "primary duty") to inform prescribers with "accurate, up-to-date information."<sup>246</sup>

The potential universe of foreseeable risks and benefits certainly includes those described on the FDA-approved labels for prescription products. But "foreseeable benefits" are not necessarily limited to those uses that have undergone the FDA approval process. If they were, off-label prescription would always be indicative of malpractice and never recognized as the standard of care.<sup>247</sup>

Even if pharmaceutical companies were motivated solely by a single-minded interest in selling drugs, dissemination of off-label information does more than merely inform a commercial transaction because of the unique role of the prescriber. Indeed, "in the fields of medicine and public health," information (even if commercial in nature) "can save lives."<sup>248</sup> It is for this reason that Congress and the FDA have not banned discussion or dissemination of off-label information outright.<sup>249</sup>

243. RESTATEMENT (SECOND) OF TORTS § 402A cmt. k (AM. LAW INST. 1965) ("There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs.").

244. See RESTATEMENT (THIRD) OF TORTS: PRODS. LIAB. § 6 cmt. b (AM. LAW INST. 1998) ("The rationale supporting this 'learned intermediary' rule is that only health-care professionals are in a position to understand the significance of the risks involved and to assess the relative advantages and disadvantages of a given form of prescription-based therapy.").

245. *Id.* (emphasis added).

246. Justice Breyer, joined by Justices Ginsburg, Sotomayor, and Kagan, asserted that "the detailer's 'primary duty' is informational, as opposed to sales-oriented," in his discussion of the Pharmaceutical Research and Manufacturers of America's "Code on Interactions with Healthcare Professionals." *Christopher v. SmithKline Beecham Corp.*, 132 S. Ct. 2156, 2177 (2012) (Breyer, J., dissenting).

247. While the FDA is responsible for determining the basis of a drug's safety and efficacy, a "physician is then responsible for making the final judgment as to which, if any, of the available drugs his patient will receive in the light of the information contained in their labeling *and other adequate scientific data available to him.*" Legal Status of Approved Labeling for Prescription Drugs, 37 Fed. Reg. 16503, 16504 (Aug. 15, 1972) (codified at 7 C.F.R. pt. 1050) (emphasis added).

248. *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2664 (2011); see also *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 366–67 (2002); *Bates v. State Bar of Ariz.*, 433 U.S. 350, 364 (1977); *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 763 (1976).

249. See *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 350 (2001) (noting that off-label use of prescription drugs "is an accepted and necessary corollary of the FDA's mission to regulate in this area without directly interfering with the practice of medicine"); FDA, RESPONDING TO UNSOLICITED REQUESTS, *supra* note 57, at 6; FDA, *Good Reprint Practices*, *supra* note 7.

In the context of pharmacists’ off-label promotion of compounded drugs directly to patients, Justice Breyer noted in his dissent that attempts to ban off-label promotion “try to assure that demand is generated doctor-to-patient-to-pharmacist, not pharmacist-to-advertisement-to-patient-to-doctor.”<sup>250</sup> While this may be a concern about direct-to-patient promotional efforts, it is irrelevant for purposes of pharmaceutical companies’ conversations with prescribers. Instead, the government bans fraudulent or deceptive commercial speech,<sup>251</sup> but medical and scientific information about off-label uses of prescription drugs is neither inherently fraudulent nor deceptive.<sup>252</sup>

CONCLUSION: DISCUSSION AND DISSEMINATION OF OFF-LABEL INFORMATION  
MAY BE *BOTH* COMMERCIAL AND . . .

Consistent with a primary focus on speaker incentives, many of the articles and opinions evaluating First Amendment protection of off-label promotion have framed the analysis in terms of an either/or choice: either off-label information is “promotional,” and therefore commercial in nature (i.e., the speaker is one affiliated with a pharmaceutical company), or it is not (i.e., the speaker is an “independent” researcher, clinician, or publication).<sup>253</sup> This dichotomy is neither consistent with the reality of the wide array of corporate conduct and speech that gets bundled into “off-label promotion” nor the Supreme Court’s understanding of the issue.<sup>254</sup> Instead, the ongoing exchange of off-label information between industry and prescribers is better framed as potentially commercial and scientific, educational, or even political speech.

The Supreme Court has recognized that “[e]ach method of communicating ideas is ‘a law unto itself’ and that law must reflect the ‘differing natures, values, abuses and dangers’ of each method.”<sup>255</sup> Where the speech in question is either unidirectionally targeted at, or exchanged with, end consumers (whether

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250. *Thompson*, 535 U.S. at 382 (Breyer, J., dissenting).

251. *Edenfield v. Fane*, 507 U.S. 761, 768 (1993); *In re R.M.J.*, 455 U.S. 191, 203 (1982); *Metro-media, Inc. v. City of San Diego*, 453 U.S. 490, 507 (1981); *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm’n of N.Y.*, 447 U.S. 557, 563–64 (1980).

252. See *United States v. Caronia*, 703 F.3d 149, 165 (2d Cir. 2012); *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 68 (D.D.C. 1998), *amended by* 36 F. Supp. 2d 16 (D.D.C. 1999), *appeal dismissed, judgment vacated in part sub nom.* *Wash. Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000).

253. E.g., Glenn C. Smith, *Avoiding Awkward Alchemy—In the Off-Label Drug Context and Beyond: Fully-Protected Independent Research Should Not Transmogrify into Mere Commercial Speech Just Because Product Manufacturers Distribute It*, 34 WAKE FOREST L. REV. 963, 966–67 (1999) (“[T]his Article uses the off-label drug controversy as a case study of the broader question whether the dissemination of product-specific research by product manufacturers should be characterized as commercial or non-commercial speech.” (footnote omitted)).

254. *Riley v. Nat’l Fed’n of the Blind of N.C., Inc.*, 487 U.S. 781, 795–96 (1988) (“It is not clear that a professional’s speech is necessarily commercial whenever it relates to that person’s financial motivation for speaking. But even assuming, without deciding, that such speech in the abstract is indeed merely ‘commercial,’ we do not believe that the speech retains its commercial character when it is inextricably intertwined with otherwise fully protected speech.” (citation omitted)).

255. *Metromedia, Inc.*, 453 U.S. at 501.

healthcare systems, insurers, or patients),<sup>256</sup> it makes sense that the speech should be considered commercial in nature.<sup>257</sup> There is no question that direct-to-consumer advertising or negotiation of quantities and prices by pharmaceutical companies is commercial speech.<sup>258</sup>

But when speech is part of an ongoing dialogue or exchange of information between a for-profit corporation and nonconsumer professionals who owe a fiduciary duty of care to their patients, a both commercial and fully protected hybrid framework is more appropriate.<sup>259</sup> This subpart of the “off-label promotion” universe would include in-person detailing, continuing education provided by companies, written correspondence between prescribers and companies, and meetings between company employees and key opinion leaders, any of which may include discussion and dissemination of off-label information. A hybrid framework is more consistent with the overall body of First Amendment precedent, which acknowledges the financial motivations of corporate speakers but also the interests and needs of nonconsumer listeners.<sup>260</sup>

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256. Healthcare systems are increasingly becoming critical gatekeepers for prescription drug sales. Rockoff, *supra* note 200 (“As hospital systems get bigger, they are putting distance between their doctors and drug sellers, making it harder for pharmaceutical companies to get quick acceptance of newly approved medicines and putting pressure on profits. Today, 42% of doctors practice as salaried employees of hospital systems, up from 24% in 2004, according to Cegedim Relationship Management, a marketing consultant. As a result, the pharmaceutical industry is shifting its sales efforts from doctors to the institutions they work for.”).

257. See Kevin Outterson, *Higher First Amendment Hurdles for Public Health Regulation*, 365 NEW ENG. J. MED. e13(1), e13(2) (2011) (“FDA regulation of direct-to-consumer advertising could be given more leeway than marketing to physicians, especially if medical education programs focused on helping physicians evaluate such claims.”).

258. This is the case, despite the Court’s pronouncement that the particular consumer’s interest in the free flow of commercial information . . . may be as keen, if not keener by far, than his interest in the day’s most urgent political debate. . . . Those whom the suppression of prescription drug price information hits the hardest are the poor, the sick, and particularly the aged. A disproportionate amount of their income tends to be spent on prescription drugs; yet they are the least able to learn, by shopping from pharmacist to pharmacist, where their scarce dollars are best spent. When drug prices vary as strikingly as they do, information as to who is charging what becomes more than a convenience. It could mean the alleviation of physical pain or the enjoyment of basic necessities. Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc., 425 U.S. 748, 763–64 (1976) (footnote omitted).

259. At least one federal appellate court has entertained the possibility of a commercial-political hybrid designation for corporate speech. Bellsouth Telecomms, Inc. v. Farris, 542 F.3d 499, 505 (6th Cir. 2008) (“Perhaps our difficulty in placing a label on the law suggests it is a hybrid one, one that implicates commercial *and* political speech, that implicates the interests of consumers *and* voters and that draws its heritage as much from protests over the Townshend Acts as from the *Wealth of Nations*.”). One opportunity for the Supreme Court to provide additional clarity on the line between commercial and political speech generated by for-profit corporations, and the level of scrutiny afforded to hybrid commercial-political speech, ended with a whimper—a dismissal of the writ of certiorari as improvidently granted—rather than a bang. See Nike, Inc. v. Kasky, 539 U.S. 654 (2003).

260. See *supra* Part II.B for further discussion on this matter. In addition, the First Amendment does not support restrictions on political speech based on a speaker’s corporate identity. Citizens United v. Fed. Election Comm’n, 558 U.S. 310, 315 (2010); First Nat’l Bank v. Bellotti, 435 U.S. 765, 777 (1978).

Prescribers need information about both on-label and off-label uses of prescription products in order to effectively treat their patients,<sup>261</sup> but the mere existence of information on prescription drug efficacy, safety, and effectiveness does not inherently lead to evidence-based clinical practice.<sup>262</sup> The historical “gap” between the best information on prescription drugs and “typical patterns of [clinical] care” still exists.<sup>263</sup> Some of the factors that contribute to the “gap” include the “complexity” and “large volume” of clinical data,<sup>264</sup> the time constraints of today’s clinical practices,<sup>265</sup> and the logistical challenges of effectively translating clinical study findings into meaningful messages relevant to patient care.<sup>266</sup> Each of these factors provides an incentive for manufacturers to incorporate prescriber education into a comprehensive marketing plan.<sup>267</sup>

The pharmaceutical industry has been a critical source of funding for the creation and dissemination of information about prescription drugs, and has been more effective than the public sector in disseminating study results.<sup>268</sup> While many of the industry’s resources have been devoted to detailing, pharmaceutical manufacturers have also underwritten much of the accredited continuing education programming required by most states’ licensing boards to maintain a license to provide healthcare<sup>269</sup> and have made substantial contributions to professional medical associations in support of their annual meetings, journals, and practice guidelines.<sup>270</sup>

As False Claims Act settlements for off-label promotion have increased, commercial support for continuing education presented by accredited providers declined, having reached its peak in 2007—when industry provided nearly \$1.25 billion for continuing education efforts (including in-kind commercial support)—

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261. Sandra H. Johnson, *Polluting Medical Judgment? False Assumptions in the Pursuit of False Claims Regarding Off-Label Prescribing*, 9 MINN. J.L. SCI. & TECH. 61, 116 (2008) (“Off-label prescribing decisions, even though stimulated by pharmaceutical detailing, may be justified and may provide essential care for patients.”).

262. Jerry Avorn & Michael Fischer, ‘Bench to Behavior’: *Translating Comparative Effectiveness Research into Improved Clinical Practice*, 29 HEALTH AFFAIRS 1891, 1895–96 (2010) [hereinafter Avorn & Fischer, *Bench to Behavior*].

263. *Id.* at 1891.

264. Michael A. Fischer & Jerry Avorn, *Academic Detailing Can Play a Key Role in Assessing and Implementing Comparative Effectiveness Research Findings*, 31 HEALTH AFFAIRS 2206, 2207 (2012) [hereinafter Fischer & Avorn, *Academic Detailing*].

265. *Id.*

266. Avorn & Fischer, *Bench to Behavior*, *supra* note 262, at 1892.

267. See Howard Brody & Donald W. Light, *The Inverse Benefit Law: How Drug Marketing Undermines Patient Safety and Public Health*, 101 AM. J. PUB. HEALTH 399, 402 (2011); Fischer & Avorn, *Academic Detailing*, *supra* note 264, at 2207.

268. Fischer & Avorn, *Academic Detailing*, *supra* note 264, at 2208.

269. Robert Steinbrook, *Financial Support of Continuing Education in the Health Professions*, in CONTINUING EDUCATION IN THE HEALTH PROFESSIONS: IMPROVING HEALTHCARE THROUGH LIFELONG LEARNING 104, 121 (Mary Hager ed., 2008), [http://macyfoundation.org/docs/macy\\_pubs/pub\\_ContEd\\_inHealthProf.pdf](http://macyfoundation.org/docs/macy_pubs/pub_ContEd_inHealthProf.pdf).

270. See David J. Rothman et al., *Professional Medical Associations and Their Relationships with Industry: A Proposal for Controlling Conflict of Interest*, 301 J. AM. MED. ASS’N 1367, 1367 (2009).

and falling more recently to less than \$675 million (excluding in-kind support) in 2012.<sup>271</sup> Over the same time period, advertising and exhibits income crept up, from \$284 million in 2007 to \$332 million in 2012.<sup>272</sup> This correlation suggests that pharmaceutical marketers may be reconsidering the value of funding continuing education in light of the government's enforcement policies for off-label promotion. Instead of prioritizing more nuanced prescriber education (whether on- or off-label), the government's current policies are driving more and more marketing dollars to on-label direct-to-consumer advertising.

Even those who have recommended the complete separation of education and marketing concede that, unless an alternative financing system is created, eliminating industry funding from continuing education "would be unacceptably disruptive for the major providers of accredited continuing medical education, including medical schools and professional societies, which together provide 68 percent of the total number of hours of this type of education."<sup>273</sup> It remains unclear what other uninterested sector is able to provide sufficient funding for continuing education on the most effective uses of prescription drugs.

When considering restrictions on in-person communications, the Supreme Court has considered listeners' ability to make "independent,"<sup>274</sup> "informed and reliable"<sup>275</sup> decisions. Where an in-person solicitation had the potential to coerce an "immediate yes-or-no answer" to an offer,<sup>276</sup> the Court allowed regulation of the speech because of a listener's diminished ability to resist the transaction. Where an in-person solicitation was more likely to facilitate independent deci-

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271. ACCREDITATION COUNCIL FOR CONTINUING MED. EDUC., ANNUAL REPORT 10 tbl.1.7 (2012), [http://acme.org/sites/default/files/630\\_2012\\_Annual\\_Report\\_20130724\\_1.pdf](http://acme.org/sites/default/files/630_2012_Annual_Report_20130724_1.pdf).

272. *Id.*

273. INST. OF MED. OF THE NAT'L ACADS., CONFLICT OF INTEREST IN MEDICAL RESEARCH, EDUCATION, AND PRACTICE 146 (Bernard Lo & Marilyn J. Field eds., 2009), [http://www.ncbi.nlm.nih.gov/books/NBK22942/pdf/Bookshelf\\_NBK22942.pdf](http://www.ncbi.nlm.nih.gov/books/NBK22942/pdf/Bookshelf_NBK22942.pdf); see also Rothman et al., *supra* note 270, at 1367 ("The overriding concern is that industry ties create conflicts of interest, both real and perceived.").

274. *Edenfield v. Fane*, 507 U.S. 761, 772 (1993) ("[T]he literature on the accounting profession suggests that the main dangers of compromised independence occur when a CPA firm is too dependent upon, or involved with, a long-standing client.").

275. *Ohralik v. Ohio State Bar Ass'n*, 436 U.S. 447, 457-58 (1978) ("In-person solicitation [by attorneys] is as likely as not to discourage persons needing counsel from engaging in a critical comparison of the 'availability, nature, and prices' of legal services, it actually may disserve the individual and societal interest . . . in facilitating 'informed and reliable decisionmaking.'" (citation omitted) (quoting *Bates v. State Bar of Ariz.*, 433 U.S. 350, 364 (1977))).

276. *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 642 (1985) ("Print advertising may convey information and ideas more or less effectively, but in most cases, it will lack the coercive force of the personal presence of a trained advocate. In addition, a printed advertisement, unlike a personal encounter initiated by an attorney, is not likely to involve pressure on the potential client for an immediate yes-or-no answer to the offer of representation." (emphasis added)); *Ohralik*, 436 U.S. at 457 (stating that in-person solicitation may be informative, but "often demands an immediate response, without providing an opportunity for comparison or reflection" (emphasis added)).

sion-making, though, the Court tended towards more rather than less speech.<sup>277</sup> In the case of off-label promotion, prescribers are a "sophisticated and experienced" audience legally and ethically required to exercise independent judgment.<sup>278</sup> Indeed, "[p]hysicians can, and often do, simply decline to meet with detailers, including detailers who use prescriber-identifying information. Doctors who wish to forgo detailing altogether are free to give 'No Solicitation' or 'No Detailing' instructions to their office managers or to receptionists at their places of work."<sup>279</sup>

To the extent that off-label promotion of prescription drugs has, in fact, caused prescribers to write more prescriptions that were harmful, unnecessary, or overly expensive (a fact that, due to all of the off-label promotion settlements, the government has never had to prove), it is a problem first with the prescribers, and second, with the pharmaceutical companies. Prescribers have the primary legal and ethical duty to care for their patients; pharmaceutical companies, as for-profit corporations, have a fiduciary duty to their shareholders. It is entirely reasonable (and consistent with the legal framework within which they operate) to assume that pharmaceutical companies will try to sell as much of their products as they can. In order for companies to "unduly influence" prescribers with financial incentives, those prescribers have to accept those incentives. In order for pharmaceutical companies to persuade prescribers through detailing, prescribers have to agree to meet with those detailers.

With more and more regulatory and insurer pressures to lower healthcare costs, prescribers do not have time to waste. In order for pharmaceutical companies to effectively market their products through detailing and continuing education, they need to provide information that prescribers perceive as valuable. Increasingly, pharmaceutical companies are restructuring their sales departments to incentivize their representatives' technical knowledge rather than the number of prescriptions written.<sup>280</sup> Under the current FDA policy, though, these repre-

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277. *E.g.*, *Edenfield*, 507 U.S. at 772 ("[T]he literature on the accounting profession suggests that the main dangers of compromised independence occur when a CPA firm is too dependent upon, or involved with, a long-standing client.").

278. *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2671 (2011) (citing *Edenfield*, 507 U.S. at 775). For the same reasons, the Federal Trade Commission Act sets advertising to physicians apart from the standard for false advertising. 15 U.S.C. § 55(a)(1) (2012) ("No advertisement of a drug shall be deemed to be false if it is disseminated only to members of the medical profession, contains no false representation of a material fact, and includes, or is accompanied in each instance by truthful disclosure of, the formula showing quantitatively each ingredient of such drug.").

279. *Sorrell*, 131 S. Ct. at 2669–70; *see also* Press Release, ZS Assocs., Inc., Even Traditionally Rep-Friendly Specialists Will See Fewer Pharmaceutical Sales Reps This Year (July 22, 2014), <http://www.zsassociates.com/about/news-and-events/even-traditionally-rep-friendly-specialists-will-see-fewer-pharmaceutical-sales-reps-this-year.aspx> ("Overall access to physicians has declined steadily since the first report in 2008, with about half (49 percent) of physicians in the U.S. placing moderate-to-severe restrictions on visits from pharma sales reps in 2014. This compares to 45 percent of prescribers who restricted rep access in 2013, 35 percent in 2012 and 23 percent in 2008.").

280. *E.g.*, Katie Thomas, *Glaxo Says It Will Stop Paying Doctors to Promote Drugs*, N.Y. TIMES (Dec. 16, 2013), [http://www.nytimes.com/2013/12/17/business/glaxo-says-it-will-stop-paying-doctors-to-promote-drugs.html?\\_r=0](http://www.nytimes.com/2013/12/17/business/glaxo-says-it-will-stop-paying-doctors-to-promote-drugs.html?_r=0) ("Beginning in 2015, Glaxo will also no longer compensate sales representatives based on the number of prescriptions doctors write, a standard practice that some have said

sentatives still risk indictment and prosecution for a strict liability federal misdemeanor if they broach or field questions about off-label use. Additionally, other public and private actors rely upon the FDA's current regulations and policies to allege False Claims Act, consumer protection, and tort violations against pharmaceutical companies.<sup>281</sup> The result is that the parties in the best position to provide prescribers with the off-label information needed to treat patients (both because pharmaceutical companies know more about their products than any other entity, and because the companies have significant financial and human resources for dissemination of off-label information) are increasingly less and less inclined to do so.

The dominant focus on pharmaceutical companies' marketing practices (rather than prescribers' decisions and actions) conflates problematic conduct with First Amendment-protected speech and minimizes the importance of the prescribers' role. Patients should reasonably expect informed independent judgment and loyalty from their prescribers. Independent judgment requires access to and consideration of truthful information from all stakeholders, along with the training, experience, and resources to evaluate it. The attempts to regulate truthful information about off-label uses of prescription drugs are misguided attempts to limit the influence of money in healthcare; the ongoing concern about off-label promotion is primarily a concern about prescriber loyalty to patients, not information.

With the increasing transparency of prescribers' acceptance of financial incentives from companies,<sup>282</sup> patients are better able to evaluate whether their healthcare providers' relationships with industry are problematic. Of course, most patients have limited time and resources to evaluate the web of financial incentives in which their healthcare is provided. As a result, it makes sense that the government should be involved in monitoring these financial incentives. But there are ways and laws to regulate the exchange of remuneration that have no First Amendment implications.<sup>283</sup> Rather than restricting the flow of information between pharmaceutical companies and prescribers, the focus should remain on the flow of financial incentives from industry to prescribers, and prescribers' acceptance of those incentives.

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pushed pharmaceutical sales officials to inappropriately promote drugs to doctors. . . . Glaxo said its sales representatives worldwide would instead be paid based on their technical knowledge, the quality of service they provided to clients to improve patient care, and the company's business performance.").

281. Greene & Noah, *supra* note 8, at 265–66.

282. See 42 U.S.C. § 1320a-7h(c)(1)(C)(ii) (2012) (mandating public availability of payments or other transfers of value between pharmaceutical companies and physicians); see also *The Facts About Open Payment Data*, CMS.GOV (June 30, 2015), <https://openpaymentsdata.cms.gov/>.

283. *E.g.*, 42 U.S.C. § 1320a-7b (providing the anti-kickback statute); *id.* § 1320a-7a (providing civil monetary penalties); *id.* § 1320a-7 (providing mandatory and permissive exclusions from Medicare and Medicaid); *id.* § 1395nn (prohibiting certain physician referrals). Query, though, at what point pharmaceutical companies' spending decisions may be considered "speech" by the current Court. See *Citizens United v. Fed. Election Comm'n*, 558 U.S. 310, 343 (2010) (explaining that restrictions on corporate and union expenditures on political campaigns have received First Amendment scrutiny).

None of this analysis is meant to suggest that the current system for disseminating information about prescription drugs is ideal; it most certainly is not.<sup>284</sup> Nor is it meant to suggest that pharmaceutical company employees and prescribers are all virtuous and trustworthy; they (like all of us) are working within webs of incentives and expectations that can cloud, or at least complicate, their best judgment. It is overly simplistic, though, to attribute the problems in our current system exclusively to for-profit corporations' creation and use of information. It is similarly simplistic to assume that FDA officials, as well-intentioned as they may be, are the unique arbiters of truth in this context, or that "truth" is limited to on-label information.<sup>285</sup> Prescribers and other healthcare providers owe the primary duty of care to patients, not the FDA, and not for-profit corporations. Our policies governing the exchange of information should put prescribers' (and, by extension, patients') needs at the forefront. Because of prescribers' need for off-label information and the Supreme Court's historical recognition that non-consumer listeners change the First Amendment analysis of information provided by financially driven speakers, the FDA should revise its policies regarding the exchange of off-label information between pharmaceutical companies and prescribers to allow freer exchange of truthful off-label information.

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284. See Lars Noah, *Medicine's Epistemology: Mapping the Haphazard Diffusion of Knowledge in the Biomedical Community*, 44 ARIZ. L. REV. 373, 376 (2002) (contending that the "biomedical research community can do a better job of generating and disseminating information, and physicians can do a better job of digesting such research while doing their best to manage any residual uncertainties").

285. Robertson, *supra* note 99, at 560 ("FDA defers to physician discretion to prescribe off label, because it remains ignorant about safety and efficacy claims until they are proven. In this realm, truth or falsity is not knowable a priori. Any knowledge of truth or falsity emerges from our economic and temporal investments, by those who have incentives to make those investments, in legal and institutional contexts that define those incentives." (footnotes omitted)).