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The FDA's Approach to Off-Label Communications: Restricting Free Speech in Medicine?

FDA & Health

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The views expressed are those of the author in her personal capacity and not in her official/professional capacity.

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Executive Summary

The FDA approves drugs as safe and effective for particular uses. As part of that process, the agency approves labeling describing the approved conditions of use. The FDA does not, however, regulate the practice of medicine: A physician may use a product that is approved for any purpose/use for any other purpose (an “off-label” use) in the practice of medicine. Although physicians may therefore seek (and talk about) information relating to off-label uses, the FDA has in place a system of speech regulation that, as a practical matter, bars any speech by the manufacturer of a drug describing or promoting a use of the drug for any use other than an on-label use — even if the information is entirely truthful and non-misleading and will help physicians better treat their patients. This can include information about well-controlled trials that do not appear in the product’s label, new analyses of existing data, and health economic information that would be useful for payers to consider in determining coverage.

As a result of the FDA’s interpretation of the Federal Food, Drug and Cosmetic Act (FDCA), manufacturers of pharmaceuticals may face severe penalties for disseminating truthful and non-misleading information about off-label uses before those uses are approved by the FDA. Indeed, some companies have paid settlements of hundreds of millions or billions of dollars in the face of threatened prosecution or trial in civil false claims cases. Governments and other private actors do not suffer the same burdens on their speech, even though the pharmaceutical manufacturer likely has the most complete, up-to-date, and useful information about the product. Moreover, even when it makes economic sense for a pharmaceutical manufacturer to seek FDA approval for a new use, the FDA can take many months or even years to approve such new uses. Patients — especially those with life-threatening conditions — cannot wait for the agency to act. Even with recent changes in the FDCA, if a new use concerns a rare disease — or the drug is off-patent — it may not be economical for the pharmaceutical manufacturer to seek approval of a new use.

This problem is particularly acute in the area of oncology. The majority of pharmaceuticals used to treat cancer patients are used off-label. Cancer patients may have little time to wait for the FDA’s views on a topic and are generally eager to undergo treatment with drugs for off-label indications for which there is some evidence of safety and effectiveness. Under the rules as written by the FDA, however, companies may be fearful that disseminating information to physicians to help them better understand these uses will lead to severe penalties. The FDA’s rules limiting the distribution of scientific information about approved pharmaceuticals thus not only inhibit innovation in the pharmaceutical industry, but also inhibit innovation in the health care industry by depriving health care providers (and patients) of truthful, non-misleading information about approved drugs. It would greatly improve pharmaceutical and health care innovation — and the state of healthcare in the US — if the FDA would permit the dissemination of truthful and non-misleading information about products that are approved for any use in a significantly broader range of circumstances.

Indeed, the FDA’s permitting the dissemination of this information is a constitutional imperative. Over the last two decades, courts have repeatedly struck down government restrictions on speech about medicines — including off-label use of medicines — as inconsistent with the First

Amendment to the United States Constitution. Although the FDA has promised to conduct a review of its regulations, policies, and guidance to better align with this case law, subsequent regulations and memoranda have instead repudiated this case law, and draft guidance has failed to address true off-label communications. The FDA has opened only two public dockets on these topics since the first major court cases were decided in the late 1990s and early 2000s.¹ However, new leadership at the FDA has recently rescinded previous proposals and signaled that the agency will be issuing new guidance that will be more sensitive to First Amendment concerns.² The time for FDA to address the permissible dissemination of truthful, non-misleading information about off-label use has come.

I. Off-Label Use is Important to the Proper Treatment of Patients

A treatment is “off-label” when the drug or device is used for another medical condition (progression of the illness or different illness) or patient type (gender or age), or is prescribed in a manner or dose different than the FDA approved.³ Off-label use of treatments is lawful, and in many cases is critical to patient care. The FDA expressly exempts off-label use from its regulations.⁴ After all, the FDA is not empowered to regulate the practice of medicine,⁵ and the agency has repeatedly acknowledged that for this reason, it does not regulate off-label use.⁶ Indeed, the FDA has recognized that “off-label uses of medical products have made valuable contributions to patient care.”⁷

¹ FDA, Docket No. 02N-0209 (2002); *see, e.g.*, *Thompson v. W. States Med. Ctr.*, 535 U.S. 357 (2002); *Washington Legal Found. v. Henney*, 56 F. Supp. 2d 81 (D.D.C. (1999)); *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. (1998)).

² Jill Wechsler, “Drug Marketing and Advertising Under Fire,” *PharmExec.com*, April 4, 2018, <http://www.pharmexec.com/drug-marketing-and-advertising-under-fire>.

³ Naomi Lopez Bauman and Christina Sandefur, “Restoring Free Speech in Medicine: How state lawmakers can overcome FDA regulations that keep doctors and payers in the dark,” *Goldwater Institute*, at 3, June 6, 2017.

⁴ 21 C.F.R. § 312.2(d) (“This part does not apply to the use in the practice of medicine for an unlabeled indication of a new drug product approved [by the FDA].”).

⁵ The Food, Drug, and Cosmetic Act expressly disclaims any intent by the federal government to regulate the practice of medicine. *See* 21 U.S.C. § 396 (2012).

⁶ *See, e.g.*, Notice of Proposed Rulemaking, *Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration*, 37 Fed. Reg. 16503 (Aug. 15, 1972) (“Once [an approved] new drug is in a local pharmacy after interstate shipment, the physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patient, or may otherwise vary the conditions of use from those approved in the package insert, without informing or obtaining the approval of the Food and Drug Administration.”); FDA, Draft Guidance, *Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices* at 2 (Dec. 2011) (“However, once a drug or medical device has been approved or cleared by FDA, generally, health care professionals can lawfully use or prescribe that product for uses or treatment indications that are not included in the product’s approved labeling”); FDA, Revised Draft Guidance, *Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices* at 6 (Feb. 2014) (“[A] health care professional can generally choose to use or prescribe an approved or cleared medical product for an unapproved use, if the off-label use is appropriate based on his or her judgment.”).

⁷ FDA, Response Letter to Citizen Petition of the Medical Information Working Group, Docket Nos. FDA-2011-P-0512 and FDA-2013-P-1079, at 7 (Jun. 6, 2014) (“MIWG Response Letter”).

In the area of oncology, off-label prescribing is even more common. As noted in the *Journal of Law and Medical Ethics*, “In oncology, . . . patient care could not proceed without off-label prescribing.”⁸ For example, a 2015 study of breast cancer patients found that over 55% of treatment regimens were off-label.⁹ And a 2016 study of older breast cancer patients (65 and older) found that 75% of treatment regimens were off-label.¹⁰

Off-label use is common outside of the oncology context as well.¹¹ For example, Amoxicillin, approved as an antibiotic for adults, is often prescribed off-label to treat ear infections in children.¹² Citalopram, a drug approved for treating depression, is sometimes prescribed off-label to treat symptoms such as stuttering, irritable bowel syndrome, and hot flashes in menopausal women.¹³ Magnesium sulfate, which is approved to prevent seizures for women in pre-eclampsia and to control seizures in eclampsia, is commonly used off-label to stop women from undergoing pre-term labor.¹⁴ Even aspirin has off-label uses; it is FDA-approved for pain, fever reduction, and cardiovascular disease, but it is sometimes used off-label to prevent coronary disease in diabetics.¹⁵ Indeed, Congress has even provided for reimbursement of off-label uses of drugs in many instances.¹⁶

As described further below, however, due to the FDA’s interpretation of the FDCA, manufacturers may face severe penalties, civil *and* criminal, for disseminating information about off-label uses — even if that information is *truthful and non-misleading* — until those uses are fully approved by the FDA. Fearful of prosecution for potentially “unlawful” speech, manufacturers may withhold medically valuable information about off-label uses, creating a counter-intuitive gap in the flow of information from pharmaceutical manufacturers, who often have the most complete, up-to-date, and useful information about a product, to prescribing practitioners whose job is to treat patients based on the most complete, up-to-date, and useful information about available products. This gap

⁸ See Rebecca Dresser & Joel Frader, *Off-Label Prescribing: A Call for Heightened Professional and Government Oversight*, 37(3) *J.L. Med. & Ethics* 476 (2009).

⁹ Sophie Hamel *et al.*, Off-label use of cancer therapies in women diagnosed with breast cancer in the United States. *Springerplus*. (2015) May 1;4:209 at 2.

¹⁰ Anne A. Eaton *et al.*, Prevalence and safety of off-label use of chemotherapeutic agents in older breast cancer patients: estimates from SEER-Medicare data, *J Natl Compr Canc Netw*. 2016 January; 14(1):57-65 at 1.

¹¹ James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions*, 53 *FOOD & DRUG L.J.* 71, 72 (1998) (“Off-label use is widespread in the medical community and often is essential to giving patients optimal medical care, both of which medical ethics, FDA, and most courts recognize.”).

¹² Rena M. Conti, Arielle C. Bernstein, Victoria M. Villaflor, Richard L. Schilsky, Meredith B. Rosenthal, and Peter B. Bach, “Prevalence of Off-Label Use and Spending in 2010 among Patent-Protected Chemotherapies in a Population-Based Cohort of Medical Oncologists,” *Journal of Clinical Oncology*, Original Report, July 16, 2016.

¹³ *Id.*; see also WebMD at <http://www.webmd.com/drugs/2/drug-8603/celexa-oral/details>.

¹⁴ Food and Drug Administration, “Magnesium Sulfate: Drug Safety Communication –Recommendation Against Prolonged Use in Pre-term Labor,” posted May 5, 2013, at <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm354603.htm>.

¹⁵ Christopher M. Wittich, Christopher M. Burkle, and William L. Lanier, “Ten Common Questions (and Their Answers) about Off-Label Drug Use,” *Mayo Clinic Proceedings* 87, no. 10 (October 2012) 982-90.

¹⁶ See 42 U.S.C. §§ 1395w-102(e)(1), (4)(A); 42 U.S.C. § 1395x(t)(2)(B)(ii)(II); 42 U.S.C. § 1396r-8(k)(6).

in the flow of information results in patients receiving potentially suboptimal care from practitioners.

II. The FDA's Position Regarding Off-Label Communications

Until 1938, federal law did not require manufacturers to submit information to the FDA as a prerequisite to marketing.¹⁷ Then, Congress passed the Federal Food, Drug, and Cosmetic Act,¹⁸ requiring manufacturers to prove that a drug was safe *before* marketing.¹⁹ Still, the law did not require federal evaluation of *efficacy*, only of safety. Gradually, however, federal law shifted to a more paternalistic approach, culminating in the 1962 Kefauver-Harris Drug Amendments to the Federal Food, Drug, and Cosmetic Act,²⁰ which required manufacturers to “provide substantial evidence of effectiveness for the product’s intended use.”²¹ These amendments were passed in reaction to the infamous incident involving Thalidomide, a sleep aid sometimes prescribed to pregnant women as a treatment for morning sickness, but was found to cause birth defects.²² The Kefauver-Harris Act imposed new rules for preapproval of medicines, including new standards for investigating new drugs for both safety and efficacy.²³

Yet that act was not matched to the concerns raised by the Thalidomide incident. Thalidomide was a safety problem, not an efficacy problem, and Thalidomide had not been approved in the U.S. due to lingering safety concerns.²⁴ Only seventeen of the more than 10,000 worldwide cases of children Thalidomide-related birth defects occurred in the U.S.,²⁵ and American consumers had been protected under the safety rules that were already on the books. Yet under the 1962 Amendments, today’s FDA tests are not just for safety, but also for efficacy.²⁶

Nevertheless, because the FDA does not regulate the practice of medicine, and because the cost and time required for approval of additional indications can be prohibitive,²⁷ off-label prescription is permitted without proof of efficacy or even full knowledge of proper dosage.

¹⁷ Michelle Meadows, *Promoting Safe and Effective Drugs for 100 Years*, FDA CONSUMER MAG., Jan.–Feb. 2006, <http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/PromotingSafeandEffectiveDrugsfor100Years/>.

¹⁸ 21 U.S.C. § 301 (2012).

¹⁹ Meadows, *supra* note 7.

²⁰ Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962).

²¹ Meadows, *supra* note 7.

²² Matthew R. Madara, *Constitutional Law—Sacrificing the Good of the Few for the Good of the Many: Denying the Terminally Ill Access to Experimental Medication*, 31 W. NEW ENG. L. REV. 535, 560 (2009).

²³ *Id.*

²⁴ *Id.*

²⁵ Linda Bren, *Frances Oldham Kelsey: FDA Medical Reviewer Leaves Her Mark on History*, FDA CONSUMER MAG., Mar.–Apr. 2001, https://web.archive.org/web/20090512235601/http://www.fda.gov/fdac/features/2001/201_kelsey.html.

²⁶ 21 U.S.C. § 355(d) (2012) (requiring both safety and efficacy for drug approval).

²⁷ In order to obtain approval for an additional indication, a supplemental drug application must be submitted to the FDA. Even if approval for an additional indication is approved, the pharmaceutical company may not be able to recoup the expense involved. Randall S. Stafford, MD, PhD, “Regulating Off-Label Drug Use – Rethinking the Role of the FDA,” *The New England Journal of Medicine* 358, no. 14 (April 3, 2008): 1427- 29. Moreover, the

Yet although the FDA has recognized the need for off-label *treatment*, the agency has historically taken the position that virtually all manufacturer off-label *communications* are illegal.²⁸ The FDCA states that a drug is misbranded unless its labeling contains “adequate directions for use.”²⁹ The FDA has interpreted this exception to apply only to directions for *lay* use, and prescription drugs by definition can only be used with healthcare provider supervision.³⁰ FDA regulations exempt prescription drugs from this requirement only if the drug’s prescribing information includes “adequate information” for use for “all purposes for which [the drug] is advertised or represented,”³¹ but the prescribing information cannot contain such information unless the FDA approves it as part of the marketing approval process.³² Thus, in the FDA’s view, promoting a drug for an unapproved use causes the drug’s labeling to lack “adequate information” for “all purposes for which it is advertised or represented,” therefore vitiating the adequate directions exemption and rendering the drug misbranded.

Further, the agency has taken the position that off-label communications violate the FDCA’s prohibition on shipment of an unapproved new drug,³³ even where the drug is approved for a separate use. Shipment in interstate commerce of a misbranded or unapproved product is a violation of the FDCA that may result in criminal penalties as well as product seizure and court injunction.³⁴ FDCA violations also may be argued to support substantial monetary penalties under the False Claims Act.³⁵ Notably, based on the FDA’s position, the above restrictions apply to drug manufacturers and their employees but not to other speakers, thus creating an information imbalance. Thus, while doctors and patients may receive unfiltered information from colleagues, contacts, and the internet, their inability to weigh this information against data from drug manufacturers paints an inaccurate or skewed picture of treatment options.

approval times for new indications are not shorter than for the original FDA approval of that drug. Joseph A. DiMasi, “Innovating by Developing New Uses of Already-Approved Drugs: Trends in the Marketing Approval of Supplemental Indications,” *Clinical Therapeutics* 35, no. 6 (June 2013): 808-18.

²⁸ There are limited exceptions: pharmaceutical manufacturers may respond to *unsolicited* questions from healthcare professionals about off-label use. However, those responses must be completed by the manufacturer’s medical affairs office, and all interactions with the provider must be documented. Pharmaceutical manufacturers are also permitted to distribute select journal articles and textbook chapters that examine and discuss off-label use if the off-label information meets certain criteria, the relationship between the distribution of information and the sponsoring drug manufacturer is disclosed, and the published material is not edited or presented in an abridged form. Food and Drug Administration, “Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs or Cleared Medical Devices,” Guidance for Industry, January 2009, <http://www.fda.gov/RegulatoryInformation/Guidances/ucm125126.htm>. But these exceptions are insufficient to ensure medical professionals receive all the necessary information. See Naomi Lopez Bauman and Christina Sandefur, “Restoring Free Speech in Medicine: How state lawmakers can overcome FDA regulations that keep doctors and payers in the dark,” Goldwater Institute, at 11-13, June 6, 2017

²⁹ FDCA § 502(f)(1).

³⁰ FDCA § 503(b)(1).

³¹ 21 C.F.R. § 201.100(c)(1).

³² 21 C.F.R. § 201.100(c)(2).

³³ FDCA § 505(a).

³⁴ FDCA §§ 301-304.

³⁵ 31 U.S.C. § 3729.

In other words, it isn't just manufacturers who share *false or misleading* information about a drug who are subject to punishment for misbranding. Even if a treatment is legal and prescribing it for off-label use is legal, it is nevertheless “misbranding” for the manufacturer to share *accurate information* about the off-label use. Thus, the FDA punishes drug companies and their employees if they promote or advertise truthful information about the legal use of a drug that the government has approved for sale. As is laid out in Part III, the FDA's position on off-label communications not only blocks doctors, patients, and payers from getting important information; it is also at odds with the First Amendment and sensible public policy.

III. First Amendment Cases Recognizing Constitutional Protection for Truthful, Non-Misleading Off-Label Communications About Medicines

Meanwhile, federal courts have recognized that manufacturers' truthful and non-misleading communications about drugs, including about off-label uses, are permissible and constitutionally protected.

As background, in the seminal case of *Central Hudson Gas & Electric Corp. v. Public Service Commission*, the United States Supreme Court held that commercial speech — which has been interpreted to include promotional speech by companies — receives First Amendment protection if it concerns a lawful activity and is not misleading.³⁶ The government may restrict such speech only if the restriction: (1) furthers a substantial government interest; (2) directly advances that interest; and (3) is not more extensive than necessary to serve that interest.³⁷

In 1998 and 1999, a court twice applied the *Central Hudson* principles to sustain the Washington Legal Foundation's First Amendment challenges to FDA restrictions on off-label communications. In the first challenge, the United States District Court for the District of Columbia (D.C. District Court) enjoined the FDA from applying certain guidance documents in a manner that restricted off-label speech, holding that the restrictions at issue were more extensive than necessary.³⁸ In the second case, the D.C. District Court struck down section 401 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) and FDA implementing regulations that restricted off-label communications, holding such provisions were too restrictive in furtherance of a substantial government interest.³⁹ The District Court determined that the government did not have a “substantial” interest in ensuring that physicians receive accurate information, stating that the government “cannot justify a restriction . . . on the paternalistic assumption that such restriction is necessary to protect the listener . . .”⁴⁰ The District Court held, however, that the government has a substantial interest in encouraging manufacturers to seek FDA-approval of off-label uses. Nevertheless, the court found that the restrictions requiring manufacturers to submit supplemental

³⁶ 447 U.S. 557, 566 (1980).

³⁷ *Id.*

³⁸ Washington Legal Found. v. Friedman, *supra* note 1.

³⁹ Washington Legal Found. v. Henney, *supra* note 1.

⁴⁰ *Id.* at 86.

applications before they could lawfully engage in off-label speech “amount[ed] to a kind of constitutional blackmail — comply with the statute or sacrifice your First Amendment rights.”⁴¹ In holding the restrictions unconstitutional as more extensive than necessary, the District Court listed a number of less restrictive alternatives available to FDA, including “more stringently enforc[ing] its statutory authority to prosecute misbranding.”⁴² On appeal of the second challenge, however, the Circuit Court dismissed the case when FDA reversed its position and argued that its guidance documents and the FDAMA restrictions were only “safe harbors” and did not independently authorize the FDA to restrict speech.⁴³ That tactic rendered the decision moot and ensured that the Supreme Court would never hear the case to resolve the underlying constitutional questions.

In 2011, the Supreme Court recognized that certain restrictions on truthful and non-misleading communications about medicines receive “heightened scrutiny.” In *Sorrell v. IMS Health Inc.*, the Court held that “[s]peech in aid of pharmaceutical marketing . . . is a form of expression protected by the Free Speech Clause of the First Amendment.”⁴⁴ In that case, the Supreme Court invalidated a Vermont law that prohibited pharmaceutical manufacturers from using prescriber-identifiable data for marketing purposes,⁴⁵ concluding that the law impermissibly distinguished between use of the data by pharmaceutical manufacturers and other parties.⁴⁶ The Court held that such speaker- or content-based restrictions are subject to heightened scrutiny.⁴⁷ After *Sorrell*, courts could apply the *Central Hudson* principles or “heightened scrutiny” in cases where a speech restriction was speaker- or content-based.

Then, in 2012, the United States Court of Appeals for the Second Circuit specifically recognized that the First Amendment protects truthful, non-misleading off-label communications.⁴⁸ In *United States v. Caronia*, the Second Circuit overturned the criminal conviction of a pharmaceutical sales representative who had been prosecuted for off-label promotion. The Court concluded that the limitation on off-label promotion was subject to heightened scrutiny, including because “it targets one kind of speaker — pharmaceutical manufacturers — while allowing others to speak without restriction,” but in any case “the government cannot justify a criminal prohibition of off-label promotion even under *Central Hudson*’s less rigorous intermediate test.”⁴⁹ The court held that the FDCA does not prohibit or criminalize truthful off-label promotion of FDA-approved prescription drugs.⁵⁰

Yet despite the apparent breadth of that decision, the FDA announced that the ruling would not significantly affect its enforcement practices. Instead, it resorted to a legal technicality: rather than

⁴¹ *Id.* at 87.

⁴² *Id.*

⁴³ *Washington Legal Found. v. Henney*, 202 F.3d 331, 335 (D.C. Cir. 2000).

⁴⁴ *Sorrell v. IMS Health Inc.*, 564 U.S. 552, 557 (2011).

⁴⁵ *Id.*

⁴⁶ *Id.* at 564.

⁴⁷ *Id.* at 569–71.

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

⁴⁹ *Id.* at 160, 163, 165.

⁵⁰ *Id.* at 168.

prosecuting off-label advertising outright, it would use off-label speech as evidence of misbranding, a maneuver that supposedly would not violate the First Amendment.⁵¹ But what is “branding” if not speech?

Then in 2015, the United States District Court for the Southern District of New York, in *Amarin v. United States*, ruled that pharmaceutical manufacturer Amarin could engage in truthful and non-misleading speech promoting the off-label use of an approved drug.⁵² Furthermore, the District Court determined that Amarin’s proposed statements were truthful and non-misleading, thus shielding Amarin from prosecution.⁵³ The Amarin case seemed on track to establish much-needed precedent to guide the pharmaceutical industry and settle the off-label speech question. But seven months later, the FDA and Amarin entered into a settlement agreement, wherein the FDA agreed: (1) “to be bound by the Court’s conclusion that Amarin may engage in truthful and non-misleading speech promoting the off-label use” of its drug, and (2) “to be bound by the Court’s conclusion that, based on the information known [at the time of the ruling],” Amarin’s proposed statements were “truthful and non-misleading.”⁵⁴ The FDA’s agreement that Amarin could engage in truthful and non-misleading off-label communications represents a significant shift in the FDA’s position on this issue.

Of course, the Amarin settlement agreement is not binding for anyone except the parties, and it only covers the treatment at issue in that case.⁵⁵ Due to the settlement, no broader precedent was set. As attorney Coleen Klasmeier observes, “Most legal issues presented by the cases never get ventilated in court or any open legal forum,” and settlements “behind closed doors” undermine “nuanced interpretation” of complex legal matters.⁵⁶ In fact, the FDA announced that its settlement “does not signify [any] position on the First Amendment and commercial speech.”⁵⁷ Thus, companies still face substantial uncertainty regarding the FDA’s broader position on off-label communications.

For example, [Vascular Solutions](#), a company that develops life-saving medical devices, was forced to undergo a five-year legal battle with the FDA over off-label communications. CEO Howard Root says of what he calls his “[unjust prosecution](#)”:

⁵¹ Eric Marshall, “FDA Explains Decision Not to Seek Rehearing in Caronia,” *Beyond Health Care Reform*, January 23, 2013, <http://beyondhealthcarereform.com/fda-explains-decision-not-to-seek-rehearing-in-caronia/>.

⁵² Opinion and Order at 69, *Amarin Pharma, Inc. v. FDA*, No. 15-3588 (S.D.N.Y. Aug. 7, 2015).

⁵³ *Id.*

⁵⁴ Proposed Stipulation and Order of Settlement at 2, *Amarin Pharma, Inc. v. FDA*, No. 15-3588 (S.D.N.Y. March 8, 2016).

⁵⁵ In February 2016, a jury in the United States District Court for the Western District of Texas acquitted the medical device company Vascular Solutions and its CEO of charges of misbranding and conspiracy based on an alleged off-label promotion, where the jury instructions made clear that truthful and non-misleading statements concerning off-label uses of approved products are not unlawful. *See United States v. Vascular Solutions, Inc.*, Cr. No. 14-926 (W.D. Tex. Feb. 25, 2016).

⁵⁶ Thomas Sullivan, “US v. Caronia, One Year Later: FDA’s Position on Off-Label Promotion Remains the Same, but Changes Are Looming,” *Policy & Medicine*, February 20, 2014, <http://www.policymed.com/2014/02/us-v-caronia-one-year-later-fdas-position-on-off-label-promotion-remains-the-same-but-changes-are-looming.html>.

⁵⁷ Eric Palmer, “With FDA Settlement, Tiny Amarin Creates Opening for Pharma in Off-Label Marketing,” *Fierce Pharma*, March 9, 2016, <http://www.fiercepharma.com/pharma/fda-settlement-tiny-amarin-creates-opening-for-pharma-off-label-marketing>.

I took the entrepreneurial plunge in 1997 when I started Vascular Solutions. Over the last 20 years, I've led the company in developing over 100 new medical devices that are used worldwide to improve the lives of patients suffering from vascular disease. In the process, we've created more than 500 well-paying American jobs and never received so much as a warning letter from the Food and Drug Administration (FDA).

But over the past five years, the Department of Justice has tried to convict me of a felony that could have put me in prison for years. My "crime"? The prosecutors thought it was "off-label" for our salespeople to talk with physicians about using just one version of just one of our more than 100 medical devices to treat perforator varicose veins rather than saphenous varicose veins.

They believed this was a felony even though our device was FDA-cleared for treating all varicose veins, over two-thirds of our salespeople never sold even one unit of it, sales constituted only 0.1 percent of our total sales and not a single patient was harmed.⁵⁸

Although Vascular Solutions was finally vindicated, the 5-year, \$25-million legal battle took a toll. The cost and uncertainty of these never-ending prosecutions will ultimately harm patients as companies won't be able to share valuable information with their doctors and insurance companies.

IV. The FDA Should Take Prompt Action to Modernize and Clarify Its Position on Off-Label Communications

The FDA's rules have not kept pace with developing First Amendment jurisprudence. In the meantime, the FDA's historical position limiting the distribution of scientific information about off-label uses of approved pharmaceuticals continues to chill constitutionally protected speech and inhibit innovation in the healthcare industry. The consequence is that doctors and patients may never learn of effective alternate uses for legally approved medications. Some providers may be failing to prescribe off-label when it is the most effective patient treatment or, perhaps of even more concern, incorrectly prescribing off-label due to a lack of the most up-to-date medical information. In the words of Samuel Nussbaum, a senior fellow at the University of Southern California's Schaeffer Center on Health Economics and Policy, "Even if a health care decisionmaker asks all of the right questions, they may still not be able to access the necessary information they need because manufacturers are hesitant to provide some information due to uncertainties in the laws and regulations that govern what they can and cannot share."⁵⁹

⁵⁸ Howard Root, "Howard Root: I'm 'not guilty,' yes, but outraged by unjust prosecution," *Minnesota Star Tribune*, Mar. 3, 2016, <http://www.startribune.com/howard-root-i-m-not-guilty-yes-but-outraged-by-unjust-prosecution/370992741/>.

⁵⁹ Dr. Samuel Nussbaum, Senior Fellow at the USC Schaeffer Center on Health Economics and Policy, statement before the Food and Drug Administration hearing on "Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products," November 9, 2016.

The healthcare industry, the pharmaceutical industry, and the state of healthcare in the United States would greatly benefit from an FDA acknowledgment that the dissemination of truthful and non-misleading off-label information about approved products is permitted in a broader range of circumstances and describe a policy identifying truthful and non-misleading communications about off-label uses.

Representatives of the pharmaceutical industry have petitioned the FDA requesting clarification regarding the regulation of off-label communications in light of the First Amendment cases described above, but so far, the FDA's response has been neither timely nor complete. In 2011, industry representatives requested clarity in the form of binding regulations regarding: (1) permissible manufacturer responses to unsolicited requests for off-label information; (2) the scope of permissible "scientific exchange" regarding off-label uses;⁶⁰ (3) permissible manufacturer interactions with formulary committees, payers, and similar entities for the purposes of ensuring coverage and reimbursement for their products, including for off-label uses; and (4) permissible dissemination of third-party clinical practice guidelines, which are used to guide important health care decisions.⁶¹ In June 2014, FDA responded by stating its plans to finalize existing guidance documents and issue additional draft guidance documents on these topics by the end of 2014.⁶² In December 2014, FDA responded again stating that it was still reviewing comments to draft guidance documents regarding off-label communications, and that its goal to issue guidance documents for these topics was now the first part of 2015.⁶³ In September 2016, FDA opened a new docket to receive comments on off-label communications more broadly and held a public hearing on the topic two months later.⁶⁴ The original notice asked for comments to be submitted by early January 2017,⁶⁵ but in December 2016, FDA further delayed that deadline to April 2017.⁶⁶

Finally, in January 2017, FDA issued a single final rule, two draft guidance documents, and a memorandum on topics related to off-label communications.⁶⁷ In reality, the draft guidance

⁶⁰ See 21 C.F.R. § 312.7(a) (noting that FDA's prohibition on sponsor promotion of an investigational drug "is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media").

⁶¹ See Medical Information Working Group, Citizen Petition, FDA-2011-P-0512, at 5–12 (Jul. 5, 2011) ("MIWG Citizen Petition").

⁶² See MIWG Response Letter, *supra* note 7, at 1–2 (Jun. 6, 2014).

⁶³ FDA, Second Response Letter to Citizen Petition of the Medical Information Working Group, Docket Nos. FDA-2011-P-0512 and FDA-2013-P-1079, at 1 (Dec. 22, 2014).

⁶⁴ See FDA, Notification of Public Hearing; Request for Comments, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products, 81 Fed. Reg. 60299 (Sept. 1, 2016); Report of Public Hearing, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products, Nov. 9, 2016, available at <http://www.fda.gov/downloads/newsevents/meetingsconferencesworkshops/ucm532489.pdf>.

⁶⁵ 81 Fed. Reg. at 60299.

⁶⁶ FDA, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products, <http://www.fda.gov/newsevents/meetingsconferencesworkshops/ucm489499.htm#writtencomments> (updated Dec. 14, 2016). See Sarah Karlin-Smith, "FDA Taking Its Time on Off-Label Promotion," Prescription Pulse, www.politico.com (Dec. 19, 2016).

⁶⁷ See Final Rule, Clarification of When Products Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses", 82 Fed. Reg. 2193 (Jan. 9, 2017); FDA, Draft Guidance, Drug and Device Manufacturer Communications With Payors, Formulary

documents do not meaningfully address off-label communications, and the final rule and the memorandum appear to repudiate recent First Amendment case law and to dismiss the decisions in *Caronia* and *Amarin* as limited to their facts.⁶⁸ Thus, not only has FDA been slow to act on off-label communications, but when it finally began to act, it failed to provide the certainty that companies need. But the agency, now under the leadership of Dr. Scott Gottlieb, has announced its plans to abandon that proposal, calling for a new study with an eye toward better compliance with the First Amendment.⁶⁹ As the FDA reevaluates its off-label policy, an analysis of where the FDA's last proposal fell short is instructive. With criminal penalties at stake, the FDA's policies continue to chill constitutionally protected, truthful and non-misleading speech.

V. The FDA's Recently Published Rule, Draft Guidance Documents, and Memorandum Fail to Meaningfully Address Off-Label Communications or First Amendment Concerns

The FDA's January 2017 now-rescinded off-label updates included draft guidance documents addressing communications with payers (Draft Guidance on Communications with Payers)⁷⁰ and communications consistent with FDA-required labeling (Draft Guidance on Communications Consistent with Labeling),⁷¹ a final rule amending the "intended use" regulations (Final Rule),⁷² and a memorandum discussing public health interests and First Amendment considerations (Memorandum).⁷³ The draft guidance documents failed to directly address off-label communications, and the final rule and memorandum represented an attempt to ignore or repudiate the First Amendment case law. If future FDA guidance and rules are to remedy the agency's constitutional deficiencies, this approach will need to be significantly altered.

First, both draft guidance documents were limited to communications that are related to or consistent with on-label uses, and both fail to recognize that truthful and non-misleading off-label information may be conveyed to prescribers.⁷⁴ The Draft Guidance on Communications with Payers

Committees, and Similar Entities—Questions and Answers (Jan. 2017) ("Draft Guidance on Communications With Payors"); FDA, Draft Guidance, Medical Product Communications That Are Consistent With FDA-Required Labeling—Questions and Answers (Jan. 2017) ("Draft Guidance on Communications Consistent With Labeling"); FDA, Memorandum, Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products (Jan. 2017).

⁶⁸ See *infra*, section V.

⁶⁹ Jill Wechsler, "Drug Marketing and Advertising Under Fire," PharmExec.com, April 4, 2018, <http://www.pharmexec.com/drug-marketing-and-advertising-under-fire>.

⁷⁰ Draft Guidance on Communications With Payors, *supra* note 67.

⁷¹ Draft Guidance on Communications Consistent With Labeling, *supra* note 67.

⁷² Final Rule, *supra* note 67.

⁷³ Memorandum, *supra* note 67.

⁷⁴ See Draft Guidance on Communication With Payors, *supra* note 67 at 5 ("Section 502(a) provides that HCEI shall not be considered false or misleading if, among other things, it 'relates to an [approved] indication.'"); Draft Guidance on Communications Consistent With Labeling, *supra* note 67 at 3 ("These general recommendations are

stated that FDA will not consider healthcare economic information (HCEI) communicated consistent with the draft guidance to be “false or misleading” or consider it as evidence of a new intended use (*i.e.*, in a prosecution for misbranding or introducing an unapproved new drug) if, among other things, it “relates” to an approved indication.⁷⁵ Thus, HCEI communicated consistent with the guidance is: (1) related to on-label, not off-label, uses; and (2) communicated only to “payer[s], formulary committee[s], or other similar entit[ies] . . . in the area of health care economic analysis,” and *not* prescribers.⁷⁶

Likewise, the Draft Guidance on Communications Consistent with Labeling described communications that FDA will consider to be consistent with on-label uses. The draft guidance created some flexibility regarding communication of on-label information but still failed to address dissemination of off-label information: “communication of information that is not consistent with the FDA-required labeling is outside the scope of these recommendations.”⁷⁷ Therefore, these draft guidance documents failed to address the key issues discussed above with respect off-label communications.

Additionally, the Memorandum and Final Rule failed to conform with First Amendment case law, and in some cases appeared to outright repudiate it. First, in the Memorandum, the FDA claimed that “[i]t makes sense for these [off-label communication] restrictions to apply only to firms” because imposing the restrictions on both firms and others would be too broad of a speech restriction.⁷⁸ This still leaves some speakers subject to criminal penalties for sharing truthful information, and the justification is flatly inconsistent with the concerns regarding speaker-based restrictions discussed in *Sorrell v. IMS Health, Inc.*⁷⁹

Second, the FDA suggested, in both the Memorandum and the preamble to the Final Rule, that it can still rely on truthful and non-misleading speech as *evidence* in a misbranding prosecution,⁸⁰ despite the statements to the contrary in *Caronia*.⁸¹ In both the Memorandum and the preamble to the Final Rule, the FDA appeared determined to ignore *Caronia*, arguing that the court: (1) “limited its analysis to addressing the constitutionality of a specific ‘construction of the FDCA’s misbranding provisions

specific to communications that are consistent with the FDA-required labeling; communication of information that is not consistent with the FDA-required labeling is outside the scope of these recommendations.”) (emphasis in original).

⁷⁵ Draft Guidance on Communications With Payors, *supra* note 67, at 5.

⁷⁶ *Id.* at 4–5 (“This guidance does not apply to dissemination of HCEI to other audiences, such as health care providers who are making individual patient prescribing decisions or consumers . . . Dissemination of HCEI to these audiences is not covered by the recommendations of this guidance.”)

⁷⁷ Draft Guidance on Communications Consistent with Labeling, *supra* note 67 at 3.

⁷⁸ See Memorandum, *supra* note 67 at 25.

⁷⁹ See section III, *supra*.

⁸⁰ 82 Fed. Reg. at 2209 (“[W]e do not agree with the assertion that the current case law allows FDA to consider speech as evidence of intended use only when it is false or misleading.”); Memorandum at 22 (“[T]he FDA Authorities do not directly prohibit or restrict speech by a firm about unapproved new uses of the firm’s medical products.”).

⁸¹ *Caronia*, 703 F.3d at 162 (finding the government prosecuted Caronia for his speech); *id.* at 168 (construing the misbranding provisions of the FDCA as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved drugs).

. . . , rather than evaluating FDA’s implementation approach”; (2) “did not consider multiple components of public health interests advanced by the FDA Authorities and FDA’s implementation approach”; and (3) “did not have the benefit of considering the significant findings” of a Canadian study regarding adverse drug events and unapproved uses.⁸²

But the outcome of *Caronia* would not have changed, even if each of these arguments were considered. First, the court *did* assess implementation in that case, finding that “the government did prosecute Caronia for his speech”⁸³ Second, while the court determined that “the government’s asserted interests in drug safety and public health are substantial,”⁸⁴ it concluded that the FDA’s speech restrictions were unconstitutional because they did not directly advance those substantial interests, nor were they narrowly drawn.⁸⁵ The additional interests cited by the FDA in the Memorandum and preamble to the Final Rule do nothing to address these flaws. Finally, the Canadian study is irrelevant, because “prohibiting off-label promotion by a pharmaceutical manufacturer while simultaneously allowing off-label use ‘paternalistically’ interferes with the ability of physicians and patients to receive potentially relevant treatment information”⁸⁶ Further, as the court concluded, “[i]f the government’s objective is to shepherd physicians to prescribe drugs only on-label, criminalizing manufacturer promotion of off-label use while permitting others to promote such use to physicians is an indirect and questionably effective means to achieve that goal.”⁸⁷

Finally, the preamble to the Final Rule indicated that knowledge of off-label use can be used as evidence of intended use for the purpose of prosecuting manufacturers for misbranding or introducing unapproved new drugs.⁸⁸ The agency stated it will not bring enforcement action based “solely” on manufacturer knowledge of off-label use. But prosecutors and qui tam litigants may abuse the FDA’s broader statements to support their view that a manufacturer who *knows* about off-label use *intends* off-label use.

Thus, the FDA’s last statement on the *Caronia* case perpetuated the agency’s semantic distortions of the court’s ruling, continuing to leave truthful speech vulnerable to unconstitutional prosecution. If the agency’s subsequent guidance does not depart from this approach and embrace truthful, non-misleading off-label speech wholeheartedly, it will continue to undermine the rule of law. Worse, failure to embrace a sensible, fair, and manageable approach to off-label speech will plague medical innovation because the uncertainty regarding what speech is and is not allowed — coupled with the severe consequences of running afoul of the FDA — will cause companies to self-censor. Consequently, doctors, payers, and patients will not be presented with all the information they need to make medical decisions. At the end of the day, the patient will be the one who suffers.

⁸² Memorandum at 23–24; 82 Fed. Reg. at 2210.

⁸³ *Caronia*, 703 F.3d at 162.

⁸⁴ *Id.* at 166.

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ *Id.* at 167.

⁸⁸ 82 Fed. Reg. at 2206 (“FDA examines all relevant evidence, which could include, among other facts, a manufacturer’s knowledge that health care providers are prescribing or using its approved/cleared medical product for an unapproved use, to determine whether there is sufficient evidence to establish a new intended use.”).

VI. States are Stepping Up to Protect Free Speech in Medicine

In response to the FDA’s lack of action, states have begun to act on their own, adopting laws to protect off-label speech where the federal system has failed to do so. While federal law typically supersedes state law, these states argue that federal law cannot preempt state law when the federal law or act *itself* is unconstitutional. The U.S. Constitution provides a floor of protection for individual rights, not a ceiling, leaving states free to enact laws that protect those rights more broadly than the federal Constitution does.⁸⁹ America’s founders envisioned the federalist system providing a “double security . . . to the rights of the people”⁹⁰ by enabling each state to “exercise its police power or its sovereign right to adopt in its own Constitution individual liberties more expansive than those conferred by the Federal Constitution.”⁹¹ As Justice William Brennan wrote nearly 40 years ago, “State constitutions, too, are a font of individual liberties, their protections often extending beyond those required by the Supreme Court’s interpretation of federal law.”⁹² This system enables states to “respond, through the enactment of positive law,” to protect the rights of citizens “without having to rely solely upon the political processes that control a remote central power.”⁹³

State constitutions already provide broader protections for free speech,⁹⁴ property rights,⁹⁵ and the right to privacy⁹⁶ than their federal counterpart. And the Supreme Court has recognized that “regulation of health and safety is ‘primarily, and historically, a matter of local concern,’” and while

⁸⁹ See, e.g., *Florida v. Powell*, 559 U.S. 50, 71 (2010) (“The federal Constitution sets the floor, not the ceiling, and [a state court] retains the ability to interpret [protections for] right[s] . . . afforded by the [state] Constitution more broadly than that afforded by its federal counterpart.”); *Kelo v. City of New London*, 545 U.S. 469, 489 (2005) (“nothing . . . precludes any State from placing further restrictions on its exercise of . . . power . . . that are stricter than the federal baseline”).

⁹⁰ *The Federalist*, No. 51, at 320 (Clinton Rossiter, ed. 1961) (James Madison); see also Arthur E. Wilmarth Jr., “The Original Purpose of the Bill of Rights,” *American Criminal Law Review*, 26, (Spring 1989): 1261 (describing how Madison “expected the states to be the most important checks against federal abuses of power”).

⁹¹ *PruneYard Shopping Center v. Robins*, 447 U.S. 74, 83 (1980).

⁹² William Brennan, “State Constitutions and the Protection of Individual Rights,” *Harvard Law Review*, 90 (1977): 489-91.

⁹³ *Bond v. United States*, 564 U.S. 211, 221 (2011).

⁹⁴ See, e.g., *Bradburn v. North Central Regional Library District*, 231 P.3d 166, 172 (Wash. 2010) (Washington’s free speech provision “is more protective of speech than the First Amendment . . . It is already settled that art. 1, § 5, is subject to independent interpretation.”); *Coleman v. City of Mesa*, 230 Ariz. 352, 361 n.5 (2012) (Arizona’s Speech Provision “is in some respects more protective of free speech rights than the First Amendment”); *Los Angeles All. for Survival v. City of Los Angeles*, 22 Cal. 4th 352, 366 (2000) (“the California liberty of speech clause is broader and more protective than the free speech clause of the First Amendment”).

⁹⁵ See, e.g., *Bailey v. Myers*, 76 P.3d 898, 903 (Ariz. App. 2003) (“the federal constitution provides considerably less protection against eminent domain than our constitution provides.”); *Board of County Com’rs of Muskogee County v. Lowery*, 136 P.3d 639, 651 (Okla. 2006) (Oklahoma’s Constitution “provide[s] private property protection to Oklahoma citizens beyond that which is afforded them by the Fifth Amendment to the U.S. Constitution”).

⁹⁶ *State v. Garza*, 2013 WL 6410445 at 2 ¶ 6 (Ariz. Ct. App. 2013) (Arizona’s Constitution “is both more explicit and more protective than its federal counterpart in ‘preserving the sanctity of homes and in creating a right of privacy’”); *Am. Acad. of Pediatrics v. Lungren*, 16 Cal. 4th 307, 326 (1997) (“the scope and application of the state constitutional right of privacy is broader and more protective of privacy than the federal constitutional right of privacy as interpreted by the federal courts.”).

federal officials can sometimes override state choices, states have “great latitude . . . to legislate as to the protection of the lives, limbs, health, comfort, and quiet of all persons.”⁹⁷

State laws protecting off-label speech do not seek to nullify federal law; rather, they seek to employ state law to protect individual rights. When the FDA silences truthful, scientific speech about lawful treatments, it is violating the constitutional right to free speech — a right protected not only by the federal Constitution but by all state constitutions as well. Thus, states can protect the rights of doctors, patients, and medical professionals to share truthful information about legal medical treatments.

State protections for off-label speech have more than just a theoretical import. States sometimes extend protections to their citizens even when those protections conflict with federal laws, and those laws co-exist without challenge in a way that results in greater freedoms for those states’ citizens. For example, in twenty-nine states, patients may use marijuana with a doctor’s prescription, despite the fact that it is a Schedule I prohibited substance under the Federal Controlled Substances Act.⁹⁸ The federal government has responded to this change by tailoring its enforcement policies to respect the authority of states to set their own policies. And state laws can be quite helpful in setting trends that inspire action in Washington, D.C. A recent example is the bipartisan, state-driven Right to Try movement, where dozens of states have passed laws protecting terminally ill patients’ right to try investigational medicines that have not yet received full approval from the FDA. In under five years, this movement has resulted in changes to FDA policies and the passage of legislation in both houses of Congress.⁹⁹ Throughout history, change has often begun at the state level.

But even if the FDA were to directly challenge state protections for off-label speech, such a move could be what is needed to finally get the core issue before the Supreme Court, since such cases would involve the states as parties, entities that would be less likely to settle a case in lieu of getting a legal precedent.

In March 2017, Governor Doug Ducey signed HB 2382, Arizona’s Free Speech in Medicine Act, which safeguards the free speech rights of manufacturers to share truthful research and information about the off-label use of FDA-approved medicines with physicians. That bill passed the Arizona State House and Senate with unanimous, bipartisan support. Arizona is the first state in the country to enact this protection, which will expand the number of treatment options in doctors’ toolkits, enhance patients’ medical autonomy, and increase access to health care.

When doctors are fully informed about the lawful treatment options available to them, they can best serve their patients’ individual needs. The law applies only to truthful communications, meaning

⁹⁷ *Gonzales v. Oregon*, 546 U.S. 243, 270-71 (2006).

⁹⁸ See “28 Legal Medical Marijuana States and DC,” PROCON.ORG, <http://medicalmarijuana.procon.org/view.resource.php?resourceID=000881> (last updated Nov. 30, 2017).

⁹⁹ Naomi Lopez Bauman, “Right to Try and the Meteoric Rise of a State Issue to the National Stage,” (Mar. 29, 2018), available at <https://indefenseofliberty.blog/2018/03/29/right-to-try-and-the-meteoric-rise-of-a-state-issue-to-the-national-stage/>.

information that is “not misleading, not contrary to fact, and consistent with generally accepted scientific principles.”

The Arizona law arguably does not go far enough to fully protect free speech, given that it only applies to communication between pharmaceutical manufacturers and licensed professionals, and does not allow pharmaceutical manufacturers to advertise off-label uses directly to the public. Patients will have to rely on doctors to receive, digest, and translate that information for their use. Nevertheless, the act is a major step forward in the effort to rescue patients and medical professionals from the FDA’s gag rule — and other states are following suit.

VII. Conclusion

As demonstrated, the FDA has failed to provide the certainty that companies need with regard to off-label communications. Without meaningful and consistent guidance and regulations, pharmaceutical manufacturers are left to guess at the FDA’s application of an off-label communications policy based largely on draft guidance documents, vague policy statements, and enforcement letters.¹⁰⁰ The FDA’s historical view that off-label communications are illegal, coupled with a stubborn refusal to accept First Amendment cases rejecting that view, leave manufacturers with no certainty that off-label communications will not expose them to significant criminal and civil liability. Consequently, the FDA’s approach continues to chill constitutionally-protected and valuable communications about off-label uses that would help doctors, and particularly oncologists, treat their patients. The time for the FDA to act is now.

The FDA should follow in the states’ footsteps, promptly extending meaningful and consistent guidance for manufacturers that is consistent with the First Amendment, recognizing that truthful and non-misleading communications about off-label uses of approved treatments are permissible. As the Supreme Court put it 40 years ago in *Virginia Board of Pharmacy v. Virginia Citizens Consumer Council*, “Information is not in itself harmful.... People will perceive their own best interests if only they are well enough informed, and ... the best means to that end is to open the channels of communication rather than to close them.”¹⁰¹ This is especially true in cases where the thing being communicated — here, prescribing off-label treatments — is itself lawful.

¹⁰⁰ See, e.g., FDA, Revised Draft Guidance, Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices (Feb. 2014); FDA, Draft Guidance, Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices (Dec. 2011). See also MIWG Citizen Petition, *supra* note 61.

¹⁰¹ *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 770 (1976).