
**WHEN TRUTH CANNOT BE PRESUMED:
THE REGULATION OF DRUG PROMOTION UNDER AN
EXPANDING FIRST AMENDMENT**

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The Food, Drug, and Cosmetic Act (FDCA) requires that, prior to marketing a drug, the manufacturer must prove that it is safe and effective for the manufacturer’s intended uses, as shown on the proposed label. Nonetheless, physicians may prescribe drugs for other “off-label” uses, and often do so. Still, manufacturers have not been allowed to promote the unproven uses in advertisements or sales pitches.

This regime is now precarious due to an onslaught of scholarly critiques, a series of Supreme Court decisions that enlarge the First Amendment, and a landmark court of appeals decision holding that the First Amendment precludes the Food and Drug Administration (FDA) from regulating off-label promotional claims. These critiques strike at the very core of the FDCA, calling into doubt the constitutionality of the entire premarket approval regime.

This Essay makes three critical contributions and offers a constructive approach to the regulation of drug promotion. First, this Essay examines the notion that “truthful” promotional claims enjoy First Amendment protection

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and illustrates how it has been central to scholarly and judicial critiques. Such critiques, however, have simply presumed the predicate of truthfulness – that the drugs are safe and effective for the newly intended uses, and further presumed that FDA is acting paternalistically to protect the public from acting upon the truth. Second, this Essay clarifies that the truth is unknown, and that this ignorance is itself the motivation for regulation. The very purpose of the FDCA is to incentivize drugmakers to invest in producing that missing knowledge. Third, this Essay highlights the way courts currently use the Daubert doctrine analogously to regulate scientific speech presented in their own courtrooms, noting that it is a prior restraint on speech that has received virtually no First Amendment scrutiny. Courts do not simply presume truthfulness.

In future FDCA enforcement actions, courts should defer to FDA's premarket approval process as the test for the truth of promotional claims, and thus the claims' status under the First Amendment. Accordingly, courts should remain in epistemic equipoise until the drugmaker proves safety and efficacy. Nonetheless, if the courts refuse to defer to the coordinate branches in the established expert regulatory process, they should instead put the burden upon the drugmaker to prove its claims true in court. Even under this fallback position, drugmakers will remain incentivized to produce the epistemic basis to support their claims of safety and efficacy. Thus the FDCA can play an appropriate role even within an enlarged conception of the First Amendment.

I. THE FDCA'S PRECARIOUS REGIME

In recent years, healthcare costs have increased substantially, now consuming one in every six dollars spent in the United States, and drugs and medical devices have been primary drivers of this growth.¹ Such consumption may be rational if it provides more value than other alternatives, and the Food, Drug, and Cosmetics Act (FDCA) is designed to increase the likelihood that consumption will be rational. Prior to the enactment of the FDCA, healthcare consumption occurred in a regime of cheap talk:

If a manufacturer wanted to put a new drug on the market, he did so. . . . There was no law that required safety testing. The manufacturer was sole judge of the therapeutic benefits he should claim for his product. If a claim was fraudulent, *and if the government could prove it*, the federal government could deal with the problem. But, a false or misleading therapeutic claim was acceptable under the law in the absence of fraud. In other words, the more ignorant the manufacturer, the more sweeping his claims for drug benefit could be.²

¹ See Christopher Robertson, *The Split Benefit: The Painless Way to Put Skin Back in the Health Care Game*, 98 CORNELL L. REV. 921, 922-25 (2013) (collecting evidence of the growth of healthcare costs and new technologies as a primary cause thereof).

² W. B. Rankin, *The Future Relationships of FDA and the Pharmaceutical Industry*, 20

That was a regime where claims as to safety and efficacy were taken to be true until proven false – what, outside the law, one might call ‘naiveté.’

The FDCA was designed to put physicians and consumers on firmer epistemic footing. Now, the FDCA requires that, prior to bringing a new drug to market, the drugmaker must submit to the Food and Drug Administration (FDA) an application with supporting evidence that proves that the chemical compound is safe and effective for a particular, intended use.³

There is an interesting conceptual, almost metaphysical, point at the core of this regime: The company’s intention that a chemical compound be used to treat a disease makes that compound a new “drug,” which then creates the burden to prove that the drug works for that intended purpose.⁴ Without such a drugmaker’s intent, the compound is just a chemical – not a drug – and the FDCA does not apply at all.⁵ In other words, “[t]o put the matter in practical terms: it is because of the ‘intended uses’ principle that hardware stores are generally free to sell bottles of turpentine, but may not label those bottles, ‘*Hamlin’s Wizard Oil: There is no Sore it will Not Heal, No Pain it will not Subdue,*’” as they did prior to the FDCA.⁶ The manufacturer’s intended uses

FOOD DRUG COSM. L.J. 632, 632 (1965) (emphasis added).

³ See 21 U.S.C. § 355(d) (2012); *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 612-14 (1973) (describing the FDCA system for new drug approval applications in light of the 1962 amendment). The FDCA provides: “No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.” 21 U.S.C. § 355(a). A “new drug” is defined as: “Any drug . . . not generally recognized . . . as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . .” *Id.* § 321(p).

⁴ See 21 U.S.C. § 321(g)(1)(B)-(C) (incorporating the intent concept in the definition of “drug”); *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 142 (2000) (“A fundamental precept of the FDCA is that any product regulated by the FDA – but not banned – must be safe for its *intended* use.” (emphasis added)); 21 C.F.R. § 201.128 (2013) (referring to the “the objective intent of the persons legally responsible for the labeling of drugs” and outlining the evidence that can show such intent). *But see* Gregory Conko, *Hidden Truth: The Perils and Protection of Off-Label Drug and Medical Device Promotion*, 21 HEALTH MATRIX 149, 159-61 (2011) (describing and criticizing this regulatory evolution).

⁵ Such a cleaving of the world through social and legal conventions is ubiquitous. See IAN HACKING, *THE SOCIAL CONSTRUCTION OF WHAT?* (2000) (discussing the ways in which the concepts we use to describe and cleave the world are often based on social and even legal conventions).

⁶ *United States v. Caronia*, 703 F.3d 149, 171 (2d Cir. 2012) (Livingston, J., dissenting); N.Y. Univ. Dep’t of Media, Culture, & Comm’n, *Traveling Medicine Show*, DEAD MEDIA ARCHIVE, http://cultureandcommunication.org/deadmedia/index.php/Traveling_Medicine_Show (last visited Jan. 3, 2014) (providing an image of such an advertisement), archived at <http://perma.cc/JF47-CLFJ>.

also define the content of labels and instructions that must accompany the product to ensure that it is not “misbranded.”⁷

Once FDA approves a drug to enter the market for a particular use (an “indication”), physicians are free to prescribe drugs for other “off-label” uses.⁸ Instead, if FDA were to proscribe off-label uses of drugs, it would interfere with physicians’ professional judgments about how to treat their patients, which is forbidden by the FDCA.⁹ Off-label usage is sometimes worthwhile, and about one-fourth of the time it is based on sound evidence of efficacy.¹⁰ In many other instances, however, off-label prescribing is a major driver of healthcare costs and presents real risks to patients that are not offset by proven benefits. For example, physicians wrote over nine million off-label prescriptions for antipsychotic drugs in 2008, amounting to about six billion dollars in the aggregate for this single class of drugs.¹¹ The side effects for these drugs include “major, rapid weight gain – forty pounds is not uncommon – Type 2 diabetes, breast development in boys, irreversible facial tics and, among the elderly, an increased risk of death.”¹² Regardless of its known risks and unknown benefits to patients, off-label promotion can be highly lucrative for the drugmakers.¹³

⁷ See 21 U.S.C. § 352 (defining “misbranding” and describing labeling requirements). Directions may be inadequate if “[s]tatements of all . . . uses for which such drug is intended” and “usual quantities [of dose] for each of the uses for which it is intended” are insufficiently specified. 21 C.F.R. § 201.5(a)-(b).

⁸ See 21 U.S.C. § 396 (“Nothing in this chapter shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship.”).

⁹ Some have argued that this discretion should be circumscribed. See, e.g., Rebecca Dresser & Joel Frader, *Off-Label Prescribing: A Call for Heightened Professional and Government Oversight*, 37 J.L. MED. & ETHICS 476, 483 (2009) (“A more direct approach to promoting patients’ interests would be to require manufacturers to submit more off-label uses for FDA review.”).

¹⁰ David C. Radley et al., *Off-Label Prescribing Among Office-Based Physicians*, 166 ARCHIVES INTERNAL MED. 1021, 1021 (2006) (showing that twenty-one percent of prescriptions are written off label and only about a quarter of those are based on adequate scientific evidence); Randall S. Stafford, *Regulating Off-Label Drug Use – Rethinking the Role of the FDA*, 358 NEW ENG. J. MED. 1427, 1427 (2008) (discussing how FDA is “relinquishing control in its new draft guidelines” in part because of the advantages of off-label prescribing, such as “innovation in clinical practice” and “earlier access to potentially valuable medications”).

¹¹ G. C. Alexander et al., *Increasing Off-Label Use of Antipsychotic Medications in the United States, 1995-2008*, 20 PHARMACOEPIDEMIOLOGY & DRUG SAFETY 177, 177 (2011) (discussing research on off-label prescriptions and 2008 prescription data).

¹² Sandra G. Boodman, *They’re Not Psychotic*, WASH. POST, Mar. 13, 2012, at E1.

¹³ See Stephanie M. Greene, *After Caronia: First Amendment Concerns in Off-Label Promotion*, 51 SAN DIEGO L. REV. (forthcoming 2014) (manuscript at 5), available at <http://ssrn.com/abstract=2375940> (discussing the off-label promotion of Neurontin, which

The regulatory logic for new uses of old drugs is the same as for the first medical use of a novel chemical compound.¹⁴ The manufacturer may not promote the drug for new uses, because doing so would evince an intention that the drug be used as such, even while the drug has not been proven effective, approved, or labeled for such use.¹⁵ The drug would then be misbranded and the introduction of it into interstate commerce would thus constitute the actus reus of a federal crime.¹⁶

This was Congress's plan. As the Senate Report on the FDCA explains, "[t]he manufacturer of the article, through his representations in connection with its sale, can determine the use to which the article is to be put."¹⁷ Indeed, what other than the manufacturer's own speech could be better evidence of its intent?¹⁸

This pattern in the law – using intent as the predicate for regulation and then using speech as evidence of intent – is quite common, and not peculiar to pharmaceutical regulation. As early as 1888, the Supreme Court affirmed a state court criminal conviction for someone who manufactured an "oleaginous substance," otherwise perfectly legal, except that he intended for it to be used as food, and thereby his manufacture of it fell under the purview of a state regulator.¹⁹ Similarly, a hollow piece of glass with a bowl on the end is illegal drug paraphernalia only if intended for such illicit uses.²⁰ An automobile is not

led to ninety percent of prescriptions being for off-label uses, with sales soaring from \$97.5 million in 1995 to approximately \$2.7 billion in 2003).

¹⁴ *But see* United States v. Caputo, 517 F.3d 935, 940 (7th Cir. 2008) (holding that the First Amendment was inapplicable because the promoted device was new, requiring FDA approval prior to marketing and thereby making the sale itself illegal). The court did not reach the question of whether off-label promotion of a device approved for another purpose would be protected by the First Amendment. *Id.*

¹⁵ *See, e.g.,* Alberty Food Prods. Co. v. United States, 185 F.2d 321, 326 (9th Cir. 1950) (holding that a drug product was misbranded because its labeling failed to state the intended use of the drug as suggested by the company in newspaper advertisements).

¹⁶ 21 U.S.C. § 352(f)(1) (2012) ("A drug or device shall be deemed to be misbranded . . . [u]nless its labeling bears (1) adequate directions for use . . .").

¹⁷ *See* United States v. Article . . . Consisting of 216 Cartoned Bottles, More or Less, Sudden Change, 409 F.2d 734, 739 n.3 (2d Cir. 1969) (quoting S. REP. NO. 74-361, at 240 (1935)); *see also* Whitaker v. Thompson, 353 F.3d 947, 953 (D.C. Cir. 2004) (holding that a product's labeling may be used to infer its intended use and thus whether it is an unapproved drug under the FDCA).

¹⁸ *See* Gregory Gentry, *Criminalizing Knowledge: The Perverse Implications of the Intended Use Regulations for Off-Label Promotion Prosecutions*, 64 FOOD & DRUG L.J. 441, 443 (2009) (discussing the regime of "objective intent," and the difficulties of attempting to criminalize mere knowledge beyond focusing on manufacturers' own statements).

¹⁹ *Powell v. Pennsylvania*, 127 U.S. 678, 679 (1888) (holding that a statute regulating the sale of an "oleaginous substance" when the seller has "intent to sell it as an article of food" is not unconstitutional).

²⁰ *See, e.g.,* Posters 'N' Things, Ltd. v. United States, 511 U.S. 513, 518 (1994) (discussing now-repealed 21 U.S.C. § 857(d), which defined "drug paraphernalia" as "items

subject to regulation by the Federal Aviation Administration, unless it is “intended to be used for flight in the air.”²¹

As to how intent can be proven, the Supreme Court has emphasized:

The First Amendment . . . does not prohibit the evidentiary use of speech to establish the elements of a crime or to prove motive or intent. Evidence of a defendant’s previous declarations or statements is commonly admitted in criminal trials subject to evidentiary rules dealing with relevancy, reliability, and the like.²²

Thus, a murder conspiracy case may turn on recordings of the defendant’s own statements that show an intent to join the conspiracy, without raising any First Amendment problems.²³ Indeed, a federal rule of evidence provides that a defendant’s speech can be used against him or her, while similar third-party speech may not be admitted.²⁴

It is notable that the FDCA does not regulate promotion of off-label uses by independent scientists, physicians, advocacy groups, or even laypersons.²⁵ Such independent information may be more reliable than the self-interested sales pitch of a pharmaceutical representative. More importantly for the law, such independent speakers have no statutory obligations with regard to labeling or distribution of drugs. Thus, their intent that the drug be used off-label is irrelevant.²⁶ The FDCA does not regulate mere speech; instead, it regulates the introduction of misbranded drugs into interstate commerce, and it

‘primarily intended . . . for use’ with controlled substances”). The current statute similarly defines drug paraphernalia as “any equipment . . . primarily intended or designed for use in . . . introducing into the human body a controlled substance . . .” 21 U.S.C. § 863 (2012).

²¹ See 14 C.F.R. § 1.1 (2013); see also *United States v. Albers*, 226 F.3d 989, 993 (9th Cir. 2000) (discussing a similar regulation at 36 C.F.R. § 1.4(a)).

²² *Wisconsin v. Mitchell*, 508 U.S. 476, 489 (1993).

²³ For a provocative argument to the contrary, see Martin H. Redish & Michael Downey, *Criminal Conspiracy as Free Expression*, 76 ALB. L. REV. 697, 698 (2013).

²⁴ FED. R. EVID. 801(d)(2) (stating that “an opposing party’s statement” is excluded from hearsay and may be admissible).

²⁵ See Ralph F. Hall & Elizabeth S. Sobotka, *Inconsistent Government Policies: Why FDA Off-Label Regulation Cannot Survive First Amendment Review Under Greater New Orleans*, 62 FOOD & DRUG L.J. 1, 9 (2007) (“Off-label speech is perfectly legal if the speaker is not affiliated with the manufacturer.”).

²⁶ Drugmakers can distribute independent scientific analyses of off-label uses, which FDA considers an educational rather than promotional activity. See FDA, 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 (2009), archived at <http://perma.cc/VQ7M-TPL4>; see also Aaron S. Kesselheim & Jerry Avorn, *The Food and Drug Administration Has the Legal Basis to Restrict Promotion of Flawed Comparative Effectiveness Research*, 31 HEALTH AFF. 2200, 2203 (2012) (arguing that FDA has the authority to close some of the loopholes that allow off-label promotion).

is the intent of the company manufacturing and selling the drug that determines whether the drug is misbranded.

Scholars have said that it is “ironic” or discriminatory that everybody except the manufacturer can promote the drug off label.²⁷ Yet the law has long recognized that manufacturers have special duties to warn and instruct with regard to their own products, duties that other manufacturers and other members of the general public do not have.²⁸ Indeed, tort law not only requires disclosure based on the manufacturer’s actual knowledge, but also imposes an affirmative duty on that particular party to undertake scientific research and disclose the results thereof.²⁹ More generally, the common law’s imposition of duty has focused upon individuals that create risks, as well as on other circumstances (such as ownership) that may put an individual in a particularly apt situation to warn or provide information to those who may be injured.³⁰

One might see the FDCA regime as a reasonable compromise between the competing needs for FDA to regulate the safety and efficacy of drugs at the threshold when they come onto the market, while also allowing physicians and their patients a measure of discretion to try drugs for new indications that are not yet proven effective. Still, scholars and attorneys have sensed that the FDCA’s regulation of off-label promotion has become precarious.³¹ At one time “commercial speech” was altogether unprotected by the First Amendment, and then it received an “intermediate scrutiny,” but that has itself “evolved into a strict scrutiny test in all but name.”³² FDA suffered a stinging defeat in the 2002 commercial speech case of *Western States Medical Center* – concerning a relatively obscure practice of pharmaceutical compounding.³³

²⁷ See Conko, *supra* note 4, at 150 (“Ironically, physicians and laymen not paid by a drug or device’s manufacturer are free to tout the benefits of off-label uses in any way and to any listener.”).

²⁸ Wendy E. Parmet & Jason A. Smith, *Free Speech and Public Health: A Population-Based Approach to the First Amendment*, 39 LOY. L.A. L. REV. 363, 421 (2006) (“The common tort law principle that manufacturers must provide warnings about the dangers associated with their product may also be viewed as a legal measure that compels speech in order to protect the public health.” (citing RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2(c) (1998))); see, e.g., Braaten v. Saberhagen Holdings, 198 P.3d 493, 504 (Wash. 2008) (limiting the duty to warn to the manufacturer’s own products).

²⁹ Golod v. Hoffman La Roche, 964 F. Supp. 841, 855 (S.D.N.Y. 1997) (“A pharmaceutical manufacturer has a duty to warn of dangers of which it knows, or in the exercise of reasonable care, should have known.”).

³⁰ See, e.g., RESTATEMENT (THIRD) OF TORTS § 7 (2010) (imposing a duty on those who create risks); *id.* § 38 (discussing affirmative duties under statutes); *id.* §§ 40-41 (discussing duties based on special relationships); *id.* §§ 42-43 (discussing duties based on undertakings); *id.* §§ 49-54 (discussing duties of land possessors).

³¹ See *infra* notes 50-61.

³² Tamara R. Piety, “A Necessary Cost of Freedom”? *The Incoherence of Sorrell v. IMS*, 64 ALA. L. REV. 1, 4 (2012).

³³ *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 357 (2002) (holding certain

Since then, FDA has avoided the Supreme Court's eye, but in related contexts, the Court has become even more expansive in its protection of First Amendment values.³⁴ The 2011 healthcare information case of *Sorrell* was particularly remarkable in its holding that a state law prohibiting the sale of data for pharmaceutical marketing purposes was unconstitutional as viewpoint discrimination.³⁵

FDA's regulatory regime for off-label promotion suffered a severe blow in the December 2012 case of *United States v. Caronia*, in which the United States Court of Appeals for the Second Circuit invoked the First Amendment to reverse a pharmaceutical sales representative's criminal conviction for conspiracy to sell a misbranded drug.³⁶ "Caronia argue[d] that he was convicted for his speech—for promoting an FDA-approved drug for off-label use"³⁷ The Second Circuit agreed with that conceptualization of the case, and said that it would "avoid constitutional difficulties by adopting a limiting interpretation" of the FDCA.³⁸ The court "construe[d] the misbranding

prohibitions on soliciting or advertising prescriptions for compounded drugs to constitute an unconstitutional restriction on commercial speech).

³⁴ See, e.g., *Agency for Int'l Dev. v. Alliance for Open Soc'y Int'l*, 133 S. Ct. 2321, 2332 (2013) (declaring that a policy requiring affirmation that prostitution is wrongful as a precondition to federal funding violated the First Amendment); *United States v. Alvarez*, 132 S. Ct. 2537, 2543 (2012) (plurality opinion) (holding that the Stolen Valor Act criminalizing false claims of receipt of military honors violated the First Amendment); *Knox v. Serv. Emps. Int'l Union, Local 1000*, 132 S. Ct. 2277, 2281 (2012) ("Public-sector unions have the right under the First Amendment to express their views on political and social issues without government interference . . . [and] employees who choose not to join a union have the same rights." (citation omitted)); *Brown v. Entm't Merch. Ass'n*, 131 S. Ct. 2729, 2731 (2011) (holding that a California law restricting the sale or rental of video games to minors violated the First Amendment); *United States v. Stevens*, 130 S. Ct. 1577, 1582, 1592 (2010) (announcing that a statute "criminaliz[ing] the commercial creation, sale, or possession of certain depictions of animal cruelty" was substantially overbroad in violation of the First Amendment); *Citizens United v. FEC*, 130 S. Ct. 876, 899 (2010) ("[I]n the context of political speech, the Government may [not] impose restrictions on certain disfavored speakers."); see also *FCC v. Fox Television Stations*, 132 S. Ct. 2307, 2309 (2012) (discussing due process issues, but addressing First Amendment values).

³⁵ *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2670-71 (2011) ("[T]he State may not seek to remove a popular but disfavored product from the marketplace by prohibiting truthful, nonmisleading advertisements that contain impressive endorsements of catchy jingles. That the State finds expression too persuasive does not permit it to quiet the speech or to burden its messengers."). See generally Piety, *supra* note 32.

³⁶ *United States v. Caronia*, 703 F.3d 149, 164 (2d Cir. 2012) ("First, we conclude that the government's construction of the FDCA's misbranding provisions imposes content- and speaker-based restrictions on speech subject to heightened scrutiny. Second, we conclude that the government cannot justify a criminal prohibition of off-label promotion even under [a] less rigorous intermediate test.").

³⁷ *Id.* at 152.

³⁸ *Id.* at 162 (quoting *Skilling v. United States*, 130 S. Ct. 2896, 2929-30 (2010)).

provisions of the FDCA as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs” – a landmark, unprecedented holding deserving closer scrutiny.³⁹

The *Caronia* case involved the powerful central nervous system depressant Xyrem (also known as the “date rape drug”), which had been approved for two specific indications based on randomized controlled trials that proved safety and efficacy in adults.⁴⁰ Nonetheless, Mr. Caronia claimed that Xyrem was a “very safe drug,” and recommended that physicians begin using Xyrem to treat a wide range of other diseases for both adults and children, including narcolepsy with cataplexy, excessive daytime and fragmented sleep, insomnia, fibromyalgia, periodic leg movement, restless leg, Parkinson’s disease, muscular sclerosis, chronic fatigue, and chronic pain.⁴¹ Mr. Caronia asserted, in other words, that the drug would be safe and effective for helping patients with all of these disparate ailments. The Government had proceeded on the theory that Caronia’s representations revealed his intention to sell Xyrem for unapproved indications, thus making the drug “misbranded” under the FDCA, as it lacks FDA approval and instructions for safe use for those other diseases.⁴² The jury was instructed on this theory.⁴³

While granting the validity of the legal theory generally, the Second Circuit rejected the application to the *Caronia* case. One reason for the rejection was that the prosecutors referred to the off-label promotion so often (“forty times”).⁴⁴ The frequency of such references suggested to the Court that Caronia’s speech was itself a crime (though not defined in any criminal code), rather than merely evidence of intent to sell a misbranded drug, the criminal statute actually charged.⁴⁵ Still, rather than limiting its holding to cases where

³⁹ *Id.* at 168. The federal courts had previously approached this question, but both parties retreated when the case reached the Court of Appeals. *See* Wash. Legal Found. v. Henney, 202 F.3d 331, 331 n.6 (D.C. Cir. 2000) (explaining that FDA conceded on oral argument that it did not seek to regulate off-label promotion directly, but reserved the right to use the same as evidence of misbranding, whereupon the Washington Legal Foundation stated that it “no longer has a constitutional objection”). Disposing of the case, the court emphasized that “[a] manufacturer, of course, may still argue that the FDA’s use of a manufacturer’s promotion of off-label uses as evidence in a particular enforcement action violates the First Amendment,” thereby reserving the issue for another day. *Id.*

⁴⁰ The *Caronia* court explained that Xyrem, whose “active ingredient is gamma-hydroxybutyrate [sic], . . . has been federally classified as the ‘date rape drug’ for its use in the commission of sexual assaults.” *Caronia*, 703 F.3d at 155.

⁴¹ *Id.* at 157.

⁴² *Id.* at 160 (stating that the government argues that the FDCA does not prohibit promotion of an approved drug for off-label uses, but rather such promotion can serve as evidence of intent in determining whether a drug is misbranded).

⁴³ *Id.* at 159.

⁴⁴ *Id.* at 159, 161 (“Thus, the government’s theory of prosecution identified Caronia’s speech alone as the proscribed conduct.”).

⁴⁵ This reasoning is perplexing because the frequency of the Government’s references to

the prosecutors use such imbalanced rhetoric, the *Caronia* court's holding used the looming First Amendment to reconstrue the FDCA itself, so that the misbranding statute no longer proscribes truthful off-label promotion at all.⁴⁶

The court made no effort to cabin its holding in any principled way. Are manufacturers now free to transport drugs in interstate commerce that are labeled for one use, or perhaps not labeled at all, while explicitly stating that the manufacturer intends other, unlabeled and unproven uses?⁴⁷ If so, the crime of "misbranding" and the entire FDCA premarket approval regime begins to seem superfluous.⁴⁸ This regime has always tipped on the fulcrum of the manufacturer's spoken intention that the chemical compound be used to treat a particular disease, which is what makes it a drug in the first place.⁴⁹ Now, if such spoken words are off limits for regulators, the products themselves fall outside the regulation of drugs, and into the no-man's land of medical quackery, which motivated the enactment of the FDCA in the first place.

Opinion leaders and scientific journal editors have expressed concern about the *Caronia* decision and the trend that it extends, as the latest in a wave of litigation and scholarship calling into question the constitutionality of FDA's regulatory regime.⁵⁰ The head of the Cleveland Clinic called the legitimation

Caronia's off-label promotion does not reveal *why* the Government made those references (that is, whether the off-label promotion is evidence of intent (*mens rea*), or itself the *actus reus* of some crime). Furthermore, it is unclear how the Government criminalized the speech itself, when there is no such crime in the federal code, as the *Caronia* court acknowledged. *Id.* at 160 ("While the FDCA makes it a crime to misbrand or conspire to misbrand a drug, the statute and its accompanying regulations do not expressly prohibit or criminalize off-label promotion. Rather, the FDCA and FDA regulations reference 'promotion' only as evidence of a drug's intended use.").

⁴⁶ *Id.* at 169 ("We conclude simply that the government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label use of an FDA-approved drug.").

⁴⁷ The decision is perplexing in its acknowledgment that, "as a threshold matter, to warrant First Amendment protection, the speech . . . must concern lawful activity," and that "promoting off-label drug use concerns lawful activity (off-label drug use)." *Id.* at 164-65. The court was apparently focusing on the moment of consumption, not the manufacturing and selling of a misbranded drug through interstate commerce, which the statute proscribes.

⁴⁸ *See id.* at 178 (Livingston, J., dissenting) ("Under the majority's reasoning, then, any substance that may be legally sold for some purpose may be promoted by its manufacturer for any purpose – so long as the manufacturer's statements are merely unsubstantiated, rather than demonstrably false or misleading. But this reasoning would invalidate the very definitions of 'drug' and 'device' that undergird the entire FDCA.").

⁴⁹ *See supra* notes 1-7 and accompanying text.

⁵⁰ *See, e.g.,* Coleen Klasmeier & Martin H. Redish, *Off-Label Prescription Advertising, the FDA and the First Amendment: A Study in the Values of Commercial Speech Protection*, 37 AM. J.L. & MED. 315, 334 (2011); John E. Osborn, *Can I Tell You the Truth? A Comparative Perspective on Regulating Off-Label Scientific and Medical Information*, 10 YALE J. HEALTH POL'Y L. & ETHICS 299, 307 (2010).

of off-label promotion “a potential catastrophe for patients.”⁵¹ The impact will likely be far beyond the rare criminal prosecution of a drug salesperson; in practice, the regulation of drug promotion has occurred through threats to prosecute the drugmakers themselves, along with False Claims Act suits by private law enforcers – both of which have yielded many billions of dollars in settlements, and the deterrent effects that come with them.⁵²

Scholars are already predicting that, if it gets such a case, “the Supreme Court will find the FDA’s current regulatory scheme unconstitutional.”⁵³ It is perhaps understandable then that the Government declined to seek en banc or Supreme Court review.⁵⁴ In the meantime, these sorts of cases likely embolden drugmakers, thereby changing the fundamental regulatory and epistemic balance.

II. PRESUMPTIONS OF TRUTH

The *Caronia* court applied “intermediate scrutiny” for the regulation of commercial speech, whereby the Government bore the burden, but failed to show, that its criminalization of off-label prescribing “directly advanced” a governmental interest and was “narrowly drawn” for that purpose.⁵⁵ It may be tempting to wade into the commercial speech doctrine to reassess whether the *Caronia* court was correct in its “direct advancement” and “narrow tailoring” analyses, and perhaps also try to figure out whether the Supreme Court will continue to hew to intermediate scrutiny in these sorts of cases.⁵⁶

⁵¹ Editorial, *The Limits of Free Speech*, NATURE (Dec. 19, 2012), <http://www.nature.com/news/the-limits-of-free-speech-1.12062>, archived at <http://perma.cc/PY73-DC7E>; see also Marcia M. Boumil, *Off-Label Marketing and the First Amendment*, 368 NEW ENG. J. MED. 103, 103 (2013) (“On December 3, 2012, a three-judge panel of a U.S. appeals court took a controversial leap toward what some fear will be license by the courts to invalidate a host of state and federal regulations, including some applicable to health care.”).

⁵² See generally Stephanie Greene, *False Claims Act Liability for Off-Label Promotion of Pharmaceutical Products*, 110 PENN ST. L. REV. 41, 44-45 (2005); Aaron S. Kesselheim et al., *Strategies and Practices in Off-Label Marketing of Pharmaceuticals: A Retrospective Analysis of Whistleblower Complaints*, PLOS MED., Apr. 2011, at 1, 2 (“Despite regulatory restrictions on off-label marketing, the practice appears to have flourished. In 2009, Pfizer paid US \$2.3 billion to settle allegations that it marketed its drugs illegally to physicians – the largest federal health care fraud settlement in US history. In 2010, at least six other manufacturers settled charges pertaining to off-label marketing, and more were under investigation.” (endnotes omitted)).

⁵³ 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, 1946-47 (2012).

⁵⁴ See Thomas M. Burton, *FDA Won’t Appeal Ruling on Marketing as Speech*, WALL ST. J., Jan. 24, 2013, at B6 (citing FDA officials who indicated that “the government won’t appeal”).

⁵⁵ *United States v. Caronia*, 703 F.3d 149, 166-69 (2012).

⁵⁶ Many others have trod this path. See *id.* at 169 (Livingston, J., dissenting); Krista

There is a more fundamental and more interesting problem. Consider how the Second Circuit joined Mr. Caronia in framing the question: “Caronia argues that the First Amendment does not permit the government to prohibit and criminalize a pharmaceutical manufacturer’s *truthful and non-misleading* promotion of an FDA-approved drug to physicians for off-label use where such use is not itself illegal and others are permitted to engage in such speech.”⁵⁷ The court recognized the importance of this point because, “[o]f course, off-label promotion that is false or misleading is not entitled to First Amendment protection.”⁵⁸

This emphasis on truthfulness has a basis in Supreme Court jurisprudence. For example, in *Bolger*, a manufacturer of contraceptives mailed advertisements directly to consumers, and the Court emphasized the First Amendment interests at play where “a speaker desires to convey *truthful* information relevant to important social issues such as family planning and the prevention of venereal disease.”⁵⁹ In a more recent case concerning “truthful information” about physicians’ prescribing behavior, *Sorrell v. IMS*, the Supreme Court reiterated this idea.⁶⁰ At least in this domain of commercial speech, especially regarding consumer health and safety, the truthfulness of a promotional claim seems to be the predicate for constitutional protection.

In *Caronia*, this concept of “truth” figured prominently in the decision, although strikingly, the issue was not litigated: “The government [did] not contend that off-label promotion is in and of itself false or misleading.”⁶¹ Thus,

Hessler Carver, *A Global View of the First Amendment Constraints on FDA*, 63 FOOD & DRUG L.J. 151, 170-75 (2008) (providing a *Central Hudson* analysis); Greene, *supra* note 13 (manuscript at 23) (discussing Judge Livingston’s dissent in *Caronia* favorably); Luke W. Dawson, Note, *A Spoonful of Free Speech Helps the Medicine Go Down: Off-Label Speech & the First Amendment*, 99 IOWA L. REV. 803, 827-28 (2014) (assessing whether the Supreme Court’s decision in *Sorrell* implicitly overruled the *Central Hudson* regime, and its implications for off-label promotion).

⁵⁷ *Caronia*, 703 F.3d at 160 (emphasis added). This is also the way the *Caronia* court stated its holding, reconstruing “the FDCA as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs.” *Id.* at 168.

⁵⁸ *Id.* at 165 n.10 (citing *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm’n*, 447 U.S. 557, 566 (1980)); *see also* *Va. Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 771 (1976) (“Untruthful speech, commercial or otherwise, has never been protected for its own sake.”). This statement of law is called into question by the *Alvarez* case (which predated *Caronia* but was not discussed by that court). *See* *United States v. Alvarez*, 132 S. Ct. 2537, 2544-45 (2012) (plurality opinion); Tamara R. Piety, *Grounding Nike: Exposing Nike’s Quest for a Constitutional Right to Lie*, 78 TEMPLE L. REV. 151, 153 (2005) (arguing that the Supreme Court approached but then dodged the question of whether there is a constitutional right to lie).

⁵⁹ *Bolger v. Youngs Drug Prods. Corp.*, 463 U.S. 60, 69 (1983) (emphasis added).

⁶⁰ *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2670-71 (2011).

⁶¹ *Caronia*, 703 F.3d at 165 n.10.

the *Caronia* court apparently presumed that all of Mr. Caronia's off-label promotional claims were true.

Similarly, in a prominent case concerning FDA's regulation of promotional claims for dietary supplements, another Circuit acknowledged that the predicate for Constitutional scrutiny is that "[t]ruthful advertising related to lawful activities is entitled to the protections of the First Amendment."⁶² While conceding that "evidence in support of [the promotional] claim is inconclusive" (and thus the Court could not really know whether the Constitutional predicate was met), the Court nonetheless held that the First Amendment prohibited FDA from proscribing the commercial speech.⁶³

Scholars have routinely made this same presumption to get their First Amendment arguments off the ground. In his critique of FDA's regime, Osborn asks: "[W]here the challenged off-label information is *truthful*, what is the public interest in forbidding it?"⁶⁴ Likewise, Klasmeier and Redish criticize FDA's regulation in this area and offer "four core postulates of free speech theory that are indisputably contravened by the ban on off-label promotion," the first of which is: "Government may not attempt to manipulate lawful citizen behavior by means of the selective suppression of *truthful* expression advocating lawful activity."⁶⁵ Similarly, Cohen concludes her analysis writing that, "[a]lthough using a prescription drug for an unapproved purpose can be dangerous, 'the fear that people would make bad decisions if given *truthful* information cannot justify content-based burdens on speech.'"⁶⁶ It is notable that each of these critiques prominently turns on the concept of "truthfulness," and each simply presumes that the regulated promotional claims are in fact truthful.⁶⁷

Long before taking the bench, Justice Kagan wrote, "First Amendment law, as developed by the Supreme Court over the past several decades, has as its primary, though unstated, object the discovery of improper governmental motives. The doctrine comprises a series of tools to flush out illicit motives and to invalidate actions infected with them."⁶⁸ In recent years, paternalism has

⁶² *Pearson v. Shalala*, 164 F.3d 650, 655 (D.C. Cir. 1999) (quoting *In re R. M. J.*, 455 U.S. 191, 203 (1982)).

⁶³ *Id.* at 659. Instead, the court held that FDA could mandate a supplemental disclaimer notifying the consumer that the science is inconclusive and FDA "does not approve this claim." *Id.* That holding presumes that the speech is protected by the First Amendment.

⁶⁴ Osborn, *supra* note 50, at 307 (emphasis added).

⁶⁵ Klasmeier & Redish, *supra* note 50, at 350 (emphasis added).

⁶⁶ Cohen, *supra* note 53, at 1967 (quoting *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2658 (2011)).

⁶⁷ Indeed, several of the recent scholarly treatments of the constitutionality of off-label promotion highlight "truth" in their titles. See, e.g., Conko, *supra* note 4; Lars Noah, *Truth or Consequences?: Commercial Free Speech vs. Public Health Promotion (at the FDA)*, 21 HEALTH MATRIX 31 (2011).

⁶⁸ Elena Kagan, *Private Speech, Public Purpose: The Role of Governmental Motive in First Amendment Doctrine*, 63 U. CHI. L. REV. 413, 414 (1996).

become one of the most illicit of the motives.⁶⁹ These courts and commentators paint FDA as a perverse paternalist, trying to keep people from the truth.⁷⁰ In the pharmaceutical case of *Western States Medical Center*, the Supreme Court emphasized that it has long “rejected the notion that the Government has an interest in preventing the dissemination of *truthful* commercial information in order to prevent members of the public from making bad decisions with the information.”⁷¹ Accordingly, the *Caronia* court characterized “the government’s objective [as] to shepherd physicians to prescribe drugs only on-label,” as if off-label prescriptions were themselves the problem.⁷²

Thus, for the regulation of off-label promotion, the courts and commentators seem to be presuming both that they themselves know that off-label promotional claims are true, and presuming that FDA is motivated by a paternalistic desire to keep that truth out of the hands of consumers. As it happens, neither of these presumptions is warranted.

III. THE FDCA AS AN INCENTIVE FOR KNOWLEDGE PRODUCTION

Socrates famously concluded that wisdom is knowing what you do not know, or acknowledging your own ignorance. This Part recommends some judicial wisdom, as it sketches an epistemological conception of the FDCA that can supplant the presumptions of truthfulness that currently dominate doctrine and scholarship.

First, an epistemology must identify the proposition for which a claim of truth is made. Concededly, some drug promotions may not have a “truth value” at all – for example, the giving of a free pen with a drug logo may instead build a sense of affinity between the drug representative and the doctor, without making a health claim *per se*.⁷³ Such utterances would be similar to the “puffery” that is not actionable under other consumer protections statutes.⁷⁴

⁶⁹ David A. Strauss, *Persuasion, Autonomy, and Freedom of Expression*, 91 COLUM. L. REV. 334, 334 (1991) (“[T]he government may not justify a measure restricting speech by invoking harmful consequences that are caused by the persuasiveness of the speech.”); see Noah, *supra* note 67, at 32 (discussing the paternalistic motivations of some public health regulations).

⁷⁰ See Robin Hanson, *Warning Labels as Cheap-Talk: Why Regulators Ban Drugs*, 87 J. PUB. ECON. 2013, 2014 (2003) (“Regulators are presumed to know which health aids are good and which are bad, and to keep the public from the bad ones.”).

⁷¹ *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 374 (2002) (emphasis added).

⁷² *United States v. Caronia*, 703 F.3d 149, 167 (2d Cir. 2012).

⁷³ See Kevin Outterson & Shoshana Speiser, *Deductions for Drug Ads? The Constitution Does Not Require Congress to Subsidize Direct-to-Consumer Prescription Drug Advertisements*, 52 SANTA CLARA L. REV. 457, 466 (2012) (showing that certain advertisements appeal to emotions rather than making health claims); Christopher Robertson et al., *Effect of Financial Relationships on the Behaviors of Health Care Professionals: A Review of the Evidence*, 40 J.L. MED. & ETHICS 452, 452 (2012) (discussing the impact of gifts from industry to physicians).

⁷⁴ See, e.g., *Clorox Co. P.R. v. Proctor & Gamble Commercial Co.*, 228 F.3d 24, 38 (1st

For these sorts of claimless utterances, it may be a “category mistake” for the court even to ask about truthfulness; and thus it would be unclear whether they are protected as “truthful” commercial speech at all.⁷⁵

Where the Government prosecutes a misbranding case however, it is because the utterance itself reveals an intent that the drug be used for a particular purpose, alleging a causal link between the product and a health outcome. Without that underlying meaning, there is no crime at all. Even then, one should not be too formalistic in the parsing of words. If a sales representative says, “I wish you would try this drug as a treatment for epilepsy,” the literal meaning is just a report of his personal desire for a sale. That report may be true, but only in a trivial sense. The “common-sense net impression” of such an utterance is a claim that the drug would be safe and effective for that purpose.⁷⁶ That is the core propositional content of the claim.

The many different claims that drug representatives make about a drug each raise distinct empirical questions. These claims are unlike the representations made in other domains, where the truthfulness is “easily verifiable.”⁷⁷ For example, either the attorney is admitted to practice in the advertised jurisdiction, or she is not.⁷⁸ In contrast, we do not know whether a drug promotional claim is true or false, and that information would be very costly to secure.⁷⁹ To prove the truth or falsehood of any one claim about drug-disease

Cir. 2000) (discussing “exaggerated advertising, blustering, and boasting upon which no reasonable buyer would rely”).

⁷⁵ *But see* Alexander v. Cahill, 598 F.3d 79, 95 (2d Cir. 2010) (acknowledging that the Supreme Court has “moved in the direction of greater First Amendment protection for ‘a logo or a slogan that conveys no information, other than identifying the source of the product, but that serves, to some degree, to ‘propose a commercial transaction’” (quoting *Bad Frog Brewery, Inc. v. N.Y. State Liquor Auth.*, 134 F.3d 87, 96 (2d Cir. 1998))). *See generally* GILBERT RYLE, *THE CONCEPT OF MIND* 16 (1949) (developing the concept of “category mistakes”).

⁷⁶ *Removatron Int’l Corp. v. FTC*, 884 F.2d 1489, 1497 (1st Cir. 1989) (looking to a “common-sense net impression” of an advertisement to find whether it made a representation in the context of Federal Trade Commission enforcement actions); *see also* U.C.C. § 2-315 (2012) (“Where the seller at the time of contracting has reason to know any particular purpose for which the goods are required . . . there is . . . an implied warranty that the goods shall be fit for such purpose.”).

⁷⁷ *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 645 (1985).

⁷⁸ *See In re R. M. J.*, 455 U.S. 191, 197 (1982).

⁷⁹ In a case involving the advertising of pharmaceutical prices, Justice Rehnquist presciently worried about a slippery slope towards other promotion claims, precisely the slide we are now experiencing. As Justice Rehnquist explained:

[A] pharmacist might run any of the following representative advertisements in a local newspaper: “Pain getting you down? Insist that your physician prescribe Demerol. You pay a little more than for aspirin, but you get a lot more relief.” “Can’t shake the flu? Get a prescription for Tetracycline from your doctor today.” “Don’t spend another sleepless night. Ask your doctor to prescribe Seconal without delay.” Unless the State can show that these advertisements are either actually untruthful or misleading, it

efficacy would cost millions of dollars and years of research by dozens of investigators and many thousands of patients taking the drug and/or placebo, at real risk of side effects and often at real opportunity cost, compared to other treatments the patients could have tried instead.⁸⁰

On this analysis, FDA defers to physician discretion to prescribe off label, because it remains ignorant about safety and efficacy claims until they are proven.⁸¹ In this realm, truth or falsity is not knowable a priori.⁸² 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. The courts should embrace this more pragmatic and situated notion of ‘truth.’⁸³

presumably is not free to restrict in any way commercial efforts on the part of those who profit from the sale of prescription drugs to put them in the widest possible circulation.

Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc., 425 U.S. 748, 788 (1976) (Rehnquist, J., dissenting).

⁸⁰ See generally Michael Dickson & Jean Paul Gagnon, *Key Factors in the Rising Cost of New Drug Discovery and Development*, 3 NATURE REVIEWS DRUG DISCOVERY 417 (2004).

⁸¹ See *Use of Approved Drugs for Unlabeled Indications*, 12 FDA DRUG BULL. 4, 4-5 (1982), cited in 59 Fed. Reg. 59,820, 59,821 (Nov. 18, 1994) (“‘[U]nlabeled’ uses may be appropriate and rational in certain circumstances, and may, in fact reflect approaches to drug therapy that have been extensively reported in medical literature. . . . Valid new uses for drugs already on the market are often first discovered through serendipitous observations and therapeutic innovations”); Klasmeier & Redish, *supra* note 50, at 318 (collecting sources for the proposition that “[g]overnment officials have themselves often openly acknowledged the benefits of off-label uses”). In other cases, the falsity of the off-label promotional claims is more obvious, and prosecutors make such arguments. See generally Miguel A. Lopez, *The Informational and Institutional Theories of Off-Label Promotion*, 49 SAN DIEGO L. REV. 913, 923-25 (2012) (discussing prosecutions under this “informational theory,” where the government targets falsehood as such, distinct from the “institutional theory,” which focuses on the integrity of the regulatory process).

⁸² Charles S. Peirce, *How to Make Our Ideas Clear*, 12 POPULAR SCI. MONTHLY 286, 286-302 (1878) (distinguishing the method of apriority from the method of science). As pragmatist philosopher Hilary Putnam has explained: “We don’t have notions of the ‘existence’ of things or of the ‘truth’ of statements that are independent of the versions we construct and of the procedures and practices that give sense to talk of ‘existence’ and ‘truth’ within those versions.” Hilary Putnam, *Why Reason Can’t Be Naturalized*, 52 SYNTHESIS 3, 4 (1982).

⁸³ See JOHN DEWEY, LOGIC: THE THEORY OF INQUIRY 9 (1938) (utilizing the concept of “warranted assertion”); DAVID L. HILDEBRAND, BEYOND REALISM AND ANTI-REALISM: JOHN DEWEY AND THE NEOPRAGMATISTS 24 (Herman J. Saatkamp, Jr. et al. eds., 2003) (describing the epistemology of John Dewey as holding that knowledge “is the result of situated processes that were initiated to respond to specific problems”).

In this sense, the FDCA does not exist to police the truth. Instead, the FDCA exists to provide and protect an epistemic and economic process of research and discovery, one that helps physicians make more rational decisions.⁸⁴

Einer Elhauge has described a “field of dreams” problem, where healthcare consumption grows towards whatever innovating product is created, regardless of whether its benefits are worth its price.⁸⁵ The market fails to create rational incentives when insurers and consumers are unable to assess those benefits, which is precisely the problem in the off-label domain, where nothing has been proven.⁸⁶ That knowledge of benefits must be produced, and paid for, by someone. “Information is needed to make product markets perform optimally, but if sellers are to provide that information then they must be given an incentive to do so.”⁸⁷

This is a regime where the drugmaker’s talk is cheap. Severely ill patients may be particularly desperate and vulnerable to medical quackery.⁸⁸ Anecdotes about this or that chemical treating this or that disease can accumulate for decades, without physicians ever learning the truth with regard to safety and efficacy⁸⁹:

Throughout the 1980s and 1990s, for example, American doctors prescribed an unapproved combination of estrogen and progestin to millions of post-menopausal women in the expectation that this hormone replacement therapy would help prevent bone loss and relieve menopause symptoms. A comprehensive study published in 2002, however, revealed that the off-label combination could increase the risk of breast cancer, heart attacks, strokes, and blood clots.⁹⁰

⁸⁴ See Dresser & Frader, *supra* note 9, at 483 (“The real value of government limits on off-label promotional activities is that they give manufacturers an incentive to sponsor the research needed to determine whether off-label uses are safe and effective.”).

⁸⁵ Einer Elhauge, *The Limited Regulatory Potential of Medical Technology Assessment*, 82 VA. L. REV. 1525, 1526 (1996).

⁸⁶ *Id.* at 1571-72 (developing such an argument about consumption in a domain of ignorance).

⁸⁷ Howard Beales et al., *The Efficient Regulation of Consumer Information*, 24 J.L. & ECON. 491, 504 (1981).

⁸⁸ See Katharine A. Van Tassel, *Slaying the Hydra: The History of Quack Medicine, the Obesity Epidemic and the FDA’s Battle to Regulate Dietary Supplements Marketed as Weight Loss Aids*, 6 IND. HEALTH L. REV. 203, 216 (2009) (explaining why the FDCA imposes a premarket approval process for products designed to treat sick people, but not one for products targeting healthy people).

⁸⁹ Beales et al., *supra* note 87, at 505-06 (“Disseminating false information and withholding negative information about a brand are obviously profitable in the short run, if the claims are believed and not countered by others. Although repeat purchases based on experience and reputation provide some market check on this strategy, some attributes may be learned only after long experience, if at all.”).

⁹⁰ Conko, *supra* note 4, at 156.

This is not a transparent, efficient market, where buyers can evaluate the value of products themselves. Even learned and earnest physicians are little help on their own when the underlying science is missing.⁹¹ After all, no individual physician could find it rational to perform such a randomized trial of the drug merely to assess its utility in her own practice. This is a classic collective action problem.⁹²

Tort law remedies – such as a patient’s claim for fraud – provide no incentive for drugmakers to prove efficacy of off-label uses; rather, they do just the opposite. Tort law would put the burden of proving falsity on the patient, but merely pointing to her own suboptimal outcome will not suffice.⁹³ Even when a drug *is* proven effective, it is proven for the median patient, and there is often heterogeneity within the sample of patients.⁹⁴ Even when the drugmaker makes a claim of efficacy, it is thus not making a warranty for every individual patient that the drug will work for her. So an individual plaintiff would need a sample of thousands of such patients to show that the drug was ineffective overall. Even then, it is nearly impossible to prove a negative (the null hypothesis: that the drug is not at all effective compared to a placebo).⁹⁵ At most, after investing millions of dollars, testing thousands of patients, and spending years working on it, an analyst could say that the drug’s effectiveness is likely smaller than some arbitrary amount (for example, two patients in 100), which corresponds to the top of the confidence interval.⁹⁶ A

⁹¹ See Vinay Prasad et al., *A Decade of Reversal: An Analysis of 146 Contradicted Medical Practices*, 88 MAYO CLINIC PROC. 790, 792 (2013) (showing that, of established medical practices that were tested in randomized trials, fewer than half of them were affirmed as being medically warranted). Even worse, many physicians are subject to conflicting interests, which likely bias their decisions. See Aaron S. Kesselheim et al., *Distributions of Industry Payments to Massachusetts Physicians*, 368 NEW ENG. J. MED. 2049 (2013) (showing that twenty-five percent of physicians received payments from the drug and device industry between July 2009 and December 2011); Robertson et al., *supra* note 73, at 452-63 (reviewing the evidence on the biasing impact of conflicting interests).

⁹² Similarly Elhauge has explained why governments and universities do not invest in producing cost-effectiveness information. See Elhauge, *supra* note 85, at 1578-80 (describing a political bias for short-term results and a collective action problem involving free riding across governments).

⁹³ See RESTATEMENT (SECOND) OF TORTS § 552 (1977) (requiring proof of falsity).

⁹⁴ See Anup Malani et al., *Improving the FDA Approval Process 2-3* (Univ. of Chi. Law Sch., John M. Olin Law & Econ., Working Paper No. 580, 2d Series, 2011), available at <http://ssrn.com/abstract=1945424> (“If a drug works in some patients but not others, however, the average patient standard may reject drugs that are effective for some patients.”).

⁹⁵ See D. A. Andow, *Negative and Positive Data, Statistical Power, and Confidence Intervals*, 2 ENVTL. BIOSAFETY RES. 75, 75 (2003) (“Negative data are data that do not enable us to reject our null hypothesis. Such data are often difficult to publish because it is not possible to prove the null hypothesis.”).

⁹⁶ See William C. Blackwelder, “*Proving the Null Hypothesis*” in *Clinical Trials*, 3 CONTROLLED CLINICAL TRIALS 345, 351-52 (1982) (“[W]e cannot actually show that

burden on the challenger to prove falsity is just not workable, and tort law is unhelpful for claims that a drug is ineffective for its off-label uses.⁹⁷

Of course, if the drugmaker researches efficacy of an off-label use, and thereby comes to believe that its own promotional claim is false, and such knowledge can be discovered in litigation, liability for fraud could attach. “In other words, the more ignorant the manufacturer, the more sweeping his claims for drug benefit could be.”⁹⁸

The Supreme Court has recognized that, in its enactment of the FDCA, Congress rejected the prior method of medicine by anecdote, in favor of a more robust epistemological regime, driven by a specialized regulator, who could evaluate the scientific merits of promotional claims, in a way that no individual physician or patient could.⁹⁹ The FDA itself has explained that its purpose is to create a knowledge base for the intelligent practice of medicine.¹⁰⁰ The insight here is equally applicable to the first usage of a new drug (the intention that makes it a new drug in the first place) as for subsequent uses of a drug intended by the drugmaker.¹⁰¹ If you want to promote it, prove it.

therapies are equivalent, but only that the difference between them is less than a specified quantity.”).

⁹⁷ For these purposes, I focus on claims that a drug lacks efficacy for an unapproved use, and I set aside liability for the drug being unsafe (for example, failure to warn claims). See Eric Helland et al., *Tort Liability and the Market for Prescription Drugs 1* (July 6, 2011) (unpublished manuscript, available at <http://ssrn.com/abstract=1883691>) (finding that tort liability on pharmaceutical companies improves social welfare); see also Greene, *supra* note 13 (manuscript at 4-5) (discussing the successful litigation over the off-label promotion of Neurontin).

⁹⁸ W. B. Rankin, *Future Relationships of FDA and the Pharmaceutical Industry*, 20 *FOOD DRUG COSMETIC L.J.* 632, 632 (1965) (emphasis added).

⁹⁹ *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 629 (1973) (“We agree with FDA, however, that the statutory scheme and overriding purpose of the 1962 amendments compel the conclusion that the hurdle of ‘general recognition’ of effectiveness requires at least ‘substantial evidence’ of effectiveness for approval of an NDA. In the absence of any evidence of adequate and well-controlled investigation supporting the efficacy of Lutrexin, *a fortiori* Lutrexin would be a ‘new drug’ subject to the provisions of the Act.”); see also *supra* notes 2, 3, & 17 and accompanying text (discussing the purposes of the FDCA).

¹⁰⁰ See FDA, *ADVANCING REGULATORY SCIENCE AT FDA 2* (2011), archived at <http://perma.cc/3UBL-J2CB> (“At the same time, FDA helps consumers and health care providers get the accurate and science-based information they need to make the best possible decisions about their use of medical products and foods for human and non-human animal use.”); Elhauge, *supra* note 85, at 1579 (“The firms that create new drugs and technologies are highly motivated to conduct studies proving the merit of their products, to gain both regulatory approval and market acceptance for the products they sell. It is existing technologies and old and new medical procedures for which information gathering poses the largest public good problem, since there are few private incentives for creating it.”).

¹⁰¹ See *supra* notes 2-18 and accompanying text (considering the FDCA’s regulatory

Courts and commentators have long understood that intellectual property has such an epistemic purpose: to incentivize the production and disclosure of knowledge.¹⁰² In particular, the patent laws are aimed at producing “useful” knowledge.¹⁰³ In the pharmaceutical sector, that means the manufacturer identifying “a specific disease against which the claimed compounds are alleged to be effective.”¹⁰⁴ Drugmakers receive additional periods of market exclusivity as an incentive to submit to the premarket approval process of FDA.¹⁰⁵ Such a framework of market exclusivity presumes a power to exclude; and sometimes that exclusion applies to speech.¹⁰⁶

By promoting new unproven uses for their drugs, manufacturers attempt to expropriate additional value from their legally enforced monopolies and their sunk costs of research and development.¹⁰⁷ The problem is that such unproven off-label uses can become substitutes, whose real quality is unobservable in any particular case, thereby reducing the demand for drugmakers to invest in producing and proving the efficacy of new drugs or new uses of old drugs.

framework).

¹⁰² See, e.g., *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 330-31 (1945) (“The primary purpose of our patent system is not reward of the individual but the advancement of the arts and sciences. Its inducement is directed to disclosure of advances in knowledge which will be beneficial to society; it is not a certificate of merit, but an incentive to disclosure.”); Donald F. Turner, *The Patent System and Competitive Policy*, 44 N.Y.U. L. REV. 450, 451 (1969) (“[W]ithout special inducements, our economy would probably underinvest in the production of knowledge because . . . the private reward for the production of knowledge would fall short of its value to the economy as a whole.”).

¹⁰³ 35 U.S.C. § 101 (2006) (“Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.”).

¹⁰⁴ *In re Brana*, 51 F.3d 1560, 1565 (Fed. Cir. 1995).

¹⁰⁵ 21 U.S.C. § 355(j)(5)(F) (2012) (providing data exclusivity protections to drug manufacturers who submit to the FDA approval process); 35 U.S.C. § 156 (2006 & Supp. V 2011) (providing for extension of patent term to account for regulatory delay while seeking FDA approval before the drug reaches the market).

¹⁰⁶ See *Zacchini v. Scripps-Howard Broad. Co.*, 433 U.S. 562, 575 (1977) (refusing to find a First Amendment privilege that would trump the intellectual property of a right of publicity, and explaining that “[t]he broadcast of a film of petitioner’s entire act poses a substantial threat to the economic value of that performance”).

¹⁰⁷ See Elhauge, *supra* note 85, at 1574-75 (arguing against using a patent-like system for incentivizing the creation of information about the efficacy of medical technologies, if it gave “some persons a monopoly over information about the effects of technologies they themselves did not own and cannot produce and sell”); Sally Wang, *Let the Arms Race End: Opening the Door to Flexible Drug Marketing Regulation Through an IP Justification*, JOLT DIGEST (May 25, 2012), <http://jolt.law.harvard.edu/digest/digest-comment/let-the-arms-race-end-opening-the-door-to-flexible-drug-marketing-regulation-through-an-ip-justification>, archived at <http://perma.cc/5V5U-EMTB> (arguing that the market monopoly granted by FDA justifies greater power to regulate speech in this domain).

This undermines a well-functioning market, where producers seek to find real drugs that actually work to cure disease. Similarly, the Federal Trade Commission Act is designed to combat “unfair methods of competition,” which includes a proscription on making unsubstantiated health claims.¹⁰⁸

The power to market off label thus licenses an economic shift away from research towards marketing. This is a loss. In a realm of ignorance, expenditures on marketing are zero sum; they simply redistribute wealth.¹⁰⁹ Expenditures on research are, on the other hand, positive sum, creating greater welfare. Without such a requirement that manufacturers prove efficacy and safety prior to promotion, that proof will not be secured, and zero-sum marketing predominates. This epistemic and economic motive for the FDCA, tying investments to market rewards, is much different than the paternalist one caricatured by the courts and commentators.¹¹⁰

IV. WHY COURTS CAN ACKNOWLEDGE THEIR IGNORANCE

In this light, should the courts continue to presume that off-label promotional claims are true, and grant them immunity under the First Amendment, even while the drugmaker has rationally declined to make investments in discerning and proving that truth to FDA? Arguably, the courts should decline to presume truthfulness, and decline to presume that such claims are shielded by the First Amendment as protected commercial speech.

A presumption can be appropriate for epistemic reasons – because it is a good guess, that is, the tentative belief most likely to approximate the truth for an agent lacking further information. Or a presumption may be appropriate for institutional reasons – because it is the most fair or charitable presumption, or because it properly incentivizes parties. Consider each.¹¹¹

Epistemically, the court has no direct evidence of the truth or falsity of the claim about a drug’s effectiveness for some new use, unless and until the court conducts a hearing on that question. So is there some indirect reason to

¹⁰⁸ 15 U.S.C. § 45(a)(1) (2012) (“Unfair methods of competition in or affecting commerce . . . are hereby declared unlawful.”); see *FTC v. Direct Mktg. Concepts, Inc.*, 569 F. Supp. 2d 285, 302 (D. Mass. 2008), *aff’d*, 624 F.3d 1 (1st Cir. 2010) (granting summary judgment to FTC where the promoters of a cure for cancer lacked “adequate substantiation for the claims”).

¹⁰⁹ See generally Peter S. H. Leeflang & Jaap E. Wieringa, *Modeling the Effects of Pharmaceutical Marketing*, 21 *MARKETING LETTERS* 121 (2010) (reviewing the literature on marketing more generally, but not specifically addressing marketing for unproven uses, which necessarily has lower utility than marketing for proven uses).

¹¹⁰ See Jane R. Bambauer, *Is Data Speech?*, 66 *STAN. L. REV.* (forthcoming 2014) (manuscript at 29), available at <http://ssrn.com/abstract=2231821> (distinguishing between laws that have “the very purpose of limiting knowledge,” versus those that encourage production thereof).

¹¹¹ For a more elaborate account, see Andrew Chignell, *The Ethics of Belief*, *STAN. ENCYCLOPEDIA PHIL.* (June 14, 2010), <http://plato.stanford.edu/archives/spr2013/entries/ethics-belief>, archived at <http://perma.cc/THR4-J28J>.

presume truth? One form of indirect evidence is the source of a claim, which can provide warrant for believing the claim itself. Two primary dimensions for evaluating a speaker are (a) his or her own expertise relevant to the question at hand, discounted by (b) any biases that likely skew the advice given.¹¹² In this case, we have a pharmaceutical sales representative, who lacks any significant medical or scientific expertise, but who receives a contingent payment for every unit of drug dispensed by the doctors in his region.¹¹³ The source of the off-label promotional claim is thus not reassuring, and consequently leaves belief in the claim unwarranted on this basis. This recognition may be one reason why FDA currently allows third parties to speak freely about new uses of approved drugs, but proscribes the self-interested drugmaker from doing so itself.¹¹⁴

The presumption of truth may be based on institutional values, rather than on the epistemic merits. In the institution of the judiciary, the mere fact of self-interested assertion – an “ipse dixit” – does not persuade.¹¹⁵ Instead, courts routinely use the rules of evidence to regulate the speech of the attorneys and witnesses that participate in their trials, to ensure that errant speech does not undermine the truth-seeking and other purposes of the trial process.¹¹⁶ For scientific claims in particular, courts follow the “gatekeeping” direction of the Supreme Court set forth in the *Daubert* trilogy and in Federal Rule of Evidence 702.¹¹⁷ This doctrine allows the courts to entertain in limine motions and hold preliminary hearings to determine what proposed testimony from expert witnesses is sufficiently reliable to be permissibly spoken in the presence of

¹¹² See generally Christopher Tarver Robertson, *Biased Advice*, 60 EMORY L.J. 653, 671 (2011) (explaining that “expertise and bias are two different dimensions of accuracy” in measuring epistemic asymmetry between expert and layperson).

¹¹³ *United States v. Caronia*, 703 F.3d 149, 156 (2d Cir. 2012) (“Caronia’s salary was based on his individual sales.”); see Greene, *supra* note 13 (manuscript at 5) (quoting a pharmaceutical executive encouraging salespersons to push “Neurontin for everything”).

¹¹⁴ See *supra* notes 25-27 and accompanying text (examining the policies behind the FDCA’s statutory requirement to regulate only manufacturers of drugs, while ignoring other independent persons).

¹¹⁵ The Supreme Court uses this Latin phrase for “he said” in the doctrine governing the admissibility of expert testimony. See, e.g., *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) (“But nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert.”).

¹¹⁶ See, e.g., *Lasar v. Ford Motor Co.*, 399 F.3d 1101, 1104-05 (9th Cir. 2005) (affirming sanctions against an attorney for violating an in limine order, without considering First Amendment issues).

¹¹⁷ *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 597 (1993) (describing the “gatekeeping” role of the district court judge). The *Daubert* principles are now reflected in revised Federal Rule of Evidence 702. FED. R. EVID. 702 (requiring, inter alia, that “the testimony is based on sufficient facts or data” and “is the product of reliable principles and methods”).

jurors. The proponent of a claim bears the burden of proving that the proposition is admissible, including any factual predicates such as the reliability of the evidence and methods supporting that claim.¹¹⁸ The courts' orders in limine thus become prior restraints, carefully delineating what may and may not be said, ultimately under threat of jail for contempt of court.¹¹⁹

One might cogently argue that the Framers did not mean for the enactment of the First Amendment to undermine the longstanding practice of courts regulating speech through the rules of evidence. Still, it is worthwhile to note the irony of courts telling other regulators that the First Amendment bars their efforts to regulate scientific speech, while at the same time the courts blithely use similar speech regulations to achieve the courts' own aims. Other scholars have noted, and passed over, this difficulty, saying that "no one would challenge seriously under the First Amendment" such judicial regulations of speech.¹²⁰ Indeed, research has failed to reveal a single case in which the rules of evidence have been challenged on First Amendment grounds. Still, these rules and doctrines are wise: they evince a proper reticence about presuming the truth of empirical claims.

Consider institutional bases for presumptions more broadly. In the particular setting of a criminal trial, the burden is generally upon the Government to prove the elements of any crime, which is to say that there is a presumption of innocence.¹²¹ Where falsehood is an element, the presumption is thus of truth. For example, the Ninth Circuit recently affirmed pharmaceutical company executive Scott Harkonen's conviction for wire fraud.¹²² The jury found that Harkonen issued a press release making materially false statements claiming the efficacy of a drug.¹²³ The court overruled his First Amendment objections, holding that the wire fraud statute's elements required proof that the speech

¹¹⁸ *Daubert v. Merrell Dow Pharm., Inc.*, 43 F.3d 1311, 1318 (9th Cir. 1995) (on remand) (discussing the burden of showing predicates).

¹¹⁹ *Se. Promotions, Ltd. v. Conrad*, 420 U.S. 546, 558 (1975) ("Any system of prior restraint, however, 'comes to this Court bearing a heavy presumption against its constitutional validity.'" (quoting *Bantam Books, Inc. v. Sullivan*, 372 U.S. 58, 70 (1963))).

¹²⁰ *See, e.g., Kathleen M. Sullivan, The Intersection of Free Speech and the Legal Profession: Constraints on Lawyers' First Amendment Rights*, 67 *FORDHAM L. REV.* 569, 569 (1998) ("Lawyers' freedom of speech is constrained in many ways that no one would challenge seriously under the First Amendment. Rules of evidence and procedure, bans on revealing grand jury testimony, page limits in briefs, and sanctions for frivolous pleadings, to name a few, are examples of speech limitations that are widely accepted as functional necessities in the administration of justice, much like rules of order in a town meeting.").

¹²¹ *See Coffin v. United States*, 156 U.S. 432, 453 (1895) ("The principle that there is a presumption of innocence in favor of the accused is the undoubted law, axiomatic and elementary, and its enforcement lies at the foundation of the administration of our criminal law.").

¹²² *United States v. Harkonen*, 510 F. App'x 633, 636 (9th Cir. 2013) (affirming Harkonen's wire fraud conviction for issuing a false press release).

¹²³ *Id.*

was false or fraudulent, which necessarily put the speech outside the First Amendment.¹²⁴ The presumption was overcome.

Falsity is not an element, however, in off-label promotion cases under the misbranding statute. In *Caronia*, for example, recall that the Government alleged that Mr. Caronia's representations revealed his intention to sell Xyrem for all those other diseases not listed on the manufacturer's drug label, which thus made the drug "misbranded" under the FDCA, as Xyrem lacks FDA approval and instructions for safe use for those other diseases.¹²⁵ For this crime – the only one charged – the truth or falsity of Mr. Caronia's promotional claims are irrelevant, since they need only show his intention to sell the drug for an unapproved purpose.¹²⁶ Thus, the elements of the crime do not themselves impose a burden on the Government to prove falsehood. There is no presumption of truthfulness.

In the sorts of cases that are at issue here, the question of "truthfulness" only arises as a predicate for the manufacturer's claim that the First Amendment protects his speech. Perhaps the First Amendment itself thus requires a presumption of truthfulness? Typically, "the standard First Amendment rule [is] that the burden of proof as to constitutionally relevant facts must lie on the party who would stifle the speech, not the speaker herself."¹²⁷ Still it is important to distinguish these misbranding cases from ones where the Government must concede the truthfulness of the claim, but argues that it is misleading.¹²⁸ In the domain of commercial speech, for such cases, the Supreme Court has held that the Government bears the burden of proving that the true speech is misleading.¹²⁹ That approach is sensible, given the epistemic

¹²⁴ *Id.* ("At trial, nearly everybody actually involved in the GIPF-001 clinical trial testified that the Press Release misrepresented GIPF-001's results.")

¹²⁵ See *United States v. Caronia*, 703 F.3d 149, 158 (2d Cir. 2012) (summarizing the State's argument); *supra* note 55 and accompanying text (explaining the elements and standards used in *Caronia* for off-label promotion).

¹²⁶ See *supra* notes 3-26 and accompanying text (setting out the importance of speech in this context, but only to prove intent).

¹²⁷ Neil Weinstock Netanel, *First Amendment Constraints on Copyright After Golan v. Holder*, 60 UCLA L. REV. 1082, 1113 (2013); see, e.g., *McKinney v. Alabama*, 424 U.S. 669, 683 (1976) ("There can be no question that uncertainty inheres in the definition of obscenity. . . . [T]he burden is on the State to prove obscenity. . . .").

¹²⁸ Other scholars have proposed such an argument that off-label speech is "inherently misleading." See, e.g., Greene, *supra* note 13 (manuscript at 26-41). The proposal here is distinct.

¹²⁹ See Carver, *supra* note 56, at 171-72 (providing an example of a case where the truthfulness of the claim was "easily" determined by the Court (citing *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 636, 646 (1985))); *Klasmeier & Redish*, *supra* note 50, at 345 ("But it surely does not follow that *all* claims made on behalf of off-label uses are *inherently* false or misleading."); see also *Whitaker v. Thompson*, 248 F. Supp. 2d 1, 7-8 (D.D.C. 2002) (rejecting this inherence theory for FDA regulation of nutritional claims).

value of truth and our aversion to paternalism, especially as a motivation for speech regulation.¹³⁰

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.

To shed light on this question, one can consult a series of cases addressing the crime of libel and the related civil actions of libel per se and defamation per se.¹³¹ Under the common law, still existing in many states, “when a plaintiff proves publication of words that are defamatory per se, the elements of *falsity* and malice (or fault) are *presumed*, but may be rebutted by the defendant.”¹³² In this line of case law, the ‘per se’ represents some topics, like allegations of sexual deviance or felonious activity, which are so beyond the pale of reasonable discourse that it is not necessary to require that the plaintiff prove falsehood.¹³³

The Supreme Court has addressed the question of the burden of proof in a string of cases, culminating in the 1986 case of *Philadelphia Newspapers, Inc. v. Hepps*, stating that “we hold that, at least where a *newspaper* publishes speech of *public concern*, a private-figure plaintiff cannot recover damages without also showing that the statements at issue are false.”¹³⁴ How this doctrine would apply to cases not involving newspapers, and involving commercial speech instead, remains unclear. In 2013, the Iowa Supreme Court discussed this notion at some length, extensively analyzing the pertinent United States Supreme Court decisions, and concluded that unless the speech is a matter of public concern by media defendants (such as newspapers), then the First Amendment permits courts to place the burden of proving truth on the defendant-speaker.¹³⁵ Thus the “per se” torts remain viable. In this light, it would similarly be permissible to put the burden on the drugmakers to prove the truth of their promotional claims as a predicate for any First Amendment claims they assert.

¹³⁰ See *supra* notes 68 & 110 and accompanying text (discussing paternalist motives).

¹³¹ See, e.g., *Carey v. Phipps*, 435 U.S. 247, 262 n.18 (1978) (noting the “essence” of libel per se); *Costello v. Hardy*, 864 So. 2d 129, 140-41 (La. 2004) (delineating how defamation per se places burdens).

¹³² *Costello*, 864 So. 2d at 140 (emphasis added).

¹³³ See, e.g., *Fleming v. Moore*, 275 S.E.2d 632, 635 (Va. 1981).

¹³⁴ 475 U.S. 767, 768-69 (1986) (emphasis added).

¹³⁵ *Bierman v. Weier*, 826 N.W.2d 436, 448 (Iowa 2013) (“A media defendant benefits from the bar on presumed damages and the requirement to prove fault and falsity, whereas a nonmedia defendant is subject to presumptions of damages, falsity, and malice if a traditional case of defamation per se has been established.”). *Contra* *Gilbert v. Bernard*, 4 Mass. L. Rptr. 142, 146 (Mass. Super. Ct. 1995) (rejecting the media versus nonmedia distinction between types of defendants, and holding that the burden must rest on the plaintiff, as long as the speech is of public concern).

Beyond the domain of truth and falsity, there are several related questions of who bears the burdens in First Amendment litigation. In some contexts, the First Amendment functions as an affirmative defense to an otherwise valid claim. For example, in Lanham Act cases, the defendant bears the burden to assert and prove that the use of an otherwise valid trademark is in fact protected speech.¹³⁶ Similarly, in the context of copyright law, the Supreme Court has said that to the extent that there is a First Amendment right to use copyrighted works, it is satisfied by the fair use exception, which functions as an affirmative defense.¹³⁷ In these sorts of cases, the proponent of a First Amendment defense thus bears the burden of proving its predicate.

The Supreme Court and lower courts have in some cases, however, rejected this approach of using an affirmative defense to satisfy the First Amendment. In the child pornography case of *Ashcroft v. Free Speech Coalition*, to avoid First Amendment problems “the Government relie[d] on an affirmative defense under the statute, which allows a defendant to avoid conviction for nonpossession offenses by showing that the materials were produced using only adults and were not otherwise distributed in a manner conveying the impression that they depicted real children.”¹³⁸ For that particular statute, the Supreme Court rejected the idea that the First Amendment concerns could be saved by an affirmative defense, since “the defendant is not the producer of the work, he may have no way of establishing the identity, or even the existence, of the actors.”¹³⁹ Arguably, in contrast, a drugmaker is in the optimal position to prove the truth of its own representations about the efficacy of its own drugs. Ultimately, the Court left open the question of whether an affirmative defense *could* do the work of the First Amendment, since the child pornography statute’s affirmative defense also was simply not written broadly

¹³⁶ See, e.g., *ETW Corp. v. Jireh Publ’g, Inc.*, 332 F.3d 915, 924 (6th Cir. 2003) (positing that the defendant in a Lanham Act claim “has raised the First Amendment as a defense to all of ETW’s claims, arguing that Rush’s use of Woods’s image in his painting is protected expression”); *Parks v. LaFace Records*, 329 F.3d 437, 444 (6th Cir. 2003) (referring to the First Amendment as a “defense” to a Lanham Act case).

¹³⁷ See *Harper & Row, Publishers, Inc. v. Nation Enters.*, 471 U.S. 539, 560 (1985); see also *Campbell v. Acuff-Rose Music, Inc.*, 510 U.S. 569, 590 (1994) (reiterating that fair use is an affirmative defense); Netanel, *supra* note 127, at 1113 (criticizing the notion that defendants must bear the burden of proving fair use); Ned Snow, *Proving Fair Use: Burden of Proof as Burden of Speech*, 31 CARDOZO L. REV. 1781, 1781 (2010) (criticizing this allocation of burdens in part because the “factual inquiries are often subjective and speculative”).

¹³⁸ 535 U.S. 234, 255 (2002).

¹³⁹ *Id.* at 255-56 (emphasis added); accord *Hodgkins ex rel. Hodgkins v. Peterson*, 355 F.3d 1048, 1064 (7th Cir. 2004) (“The statute restricts a minor’s access to any public forum during curfew hours, and the affirmative defense for participating in First Amendment activities does not significantly reduce the chance that a minor might be arrested for exercising his First Amendment rights.”).

enough.¹⁴⁰ The question remains open, and thus a potential route for restoring FDA's regulation of promotion.

A complete analysis of burdens and presumptions in First Amendment law would open a range of other interesting cases to explore.¹⁴¹ The foregoing suffices, however, to suggest that there is room within current constitutional doctrine to allow for a more realistic approach to truth and falsity in the regulation of off-label promotion. Concededly, however, this Essay provides a prescriptive analysis more than one that seeks to be descriptive of current case law.

The fundamental insight is this: It would be rather strange if the Constitution required the courts to adopt a presumption about the safety and efficacy of any given chemical compound for treating any given disease, a leap of faith that Congress, and FDA prudently refuse to take, and which *Daubert* and the Rules of Evidence prohibit the courts themselves from taking, in related contexts. Instead, the Constitution allows courts candidly and prudently to concede their ignorance about safety and efficacy, until given a warranted basis for belief.

CONCLUSION: THE FDCA AS THE TEST OF TRUTH

While not purporting to be a comprehensive treatment of the First Amendment issues implicated by the regulation of drug promotions, this Essay develops a few themes. First, it has shown how the FDCA's regulatory regime, like so many other areas of the law, turns on the defendant's own speech revealing its intent. Yet, this regime is precarious under an expanding First Amendment doctrine. While most clear in the domain of off-label promotion, the precariousness seems to cut even deeper, to undermine the FDCA's requirements for premarket approval. This threat motivates the project to explore whether FDA regulation of promotion could be reconstructed in a constitutionally sufficient way.

¹⁴⁰ *Ashcroft v. Free Speech Coal.*, 535 U.S. 234, 256 (2002) ("We need not decide, however, whether the Government could impose this burden on a speaker. Even if an affirmative defense can save a statute from First Amendment challenge, here the defense is incomplete and insufficient, even on its own terms.").

¹⁴¹ *See, e.g., Riley v. Nat'l Fed'n of the Blind*, 487 U.S. 781, 784 (1988) (holding unconstitutional, in the context of charitable solicitations, a state statute that regulated speech based on statutory presumptions as to the reasonableness of fees at various defined levels, and placing the burden on the speaker to instead show reasonableness); *Dun & Bradstreet, Inc. v. Greenmoss Builders, Inc.*, 472 U.S. 749, 758-63 (1985) (plurality opinion) (allowing punitive damages and utilizing a presumption of actual malice for speech proven false, which was not of public concern); *Mt. Healthy City Sch. Dist. Bd. of Educ. v. Doyle*, 429 U.S. 274, 285-87 (1977) (holding that employee seeking to invoke First Amendment protections against being fired by public employer bears the burden of proving causation, that is, that the speech was a substantial factor in causing her to be fired). *See generally* Harry P. Monaghan, *First Amendment "Due Process,"* 83 HARV. L. REV. 518, 519 (1969) ("[L]ike the substantive rules themselves, insensitive procedures can 'chill' the right to free expression.").

Second, this Essay has shown that the notion of truthfulness is at the core of many scholarly and judicial analyses in this domain, but that the notion is deployed presumptuously, without a sense for the economic and epistemic pragmatics. The truth or falsity of the drugmaker's promotional claims is unknown, largely because the drugmaker has declined to invest in making such a proof. The FDCA is designed to incentivize the drugmakers to make that investment, a function that is undermined if courts presume the truth as a predicate for providing immunity under the First Amendment. Accordingly, courts and commentators should abandon their unreflective presumptions that manufacturers' promotional claims are true. Courts should be as savvy in this domain as in any other domain concerning open scientific questions.

One potential response to this analysis would be for the courts to stop making unwarranted presumptions of truthfulness, while nonetheless deciding the cases the same way. Rather than saying that the First Amendment forbids FDA from proscribing *truthful* off-label promotional claims (even as evidence of intent to sell a misbranded drug), the courts and commentators would then boldly expand the First Amendment even further to say that it forbids FDA from proscribing promotional claims whose truth is *unknown*. Such a shift in judicial opinion-writing would have the virtue of causing courts to be more candid about what they are doing (regulating in acknowledged ignorance, rather than in naïve presumptuousness), but it would be imprudent as a matter of policy. On this emerging conception of the First Amendment, FDA could proscribe such a promotional claim only after proving it false.¹⁴² At most, perhaps FDA could require drugmakers to impose disclaimers acknowledging that the evidence is “inconclusive.”¹⁴³ But, just as in the wild days before the enactment of the FDCA, drugmakers could make whatever health claims they wanted, at least until somebody somehow proved them false.¹⁴⁴ This Essay offers a normative, epistemic, and economic argument explaining the collective action problem that no other individual would rationally invest in discovering the truth about these drugs. It is instead sensible to place this epistemic burden on the drugmaker, who can in the aggregate reap the financial benefits of such new uses, when it chooses to promote them.

It bears emphasis that this is not a generalized argument that speakers should always bear the burden of proving the truth of their claims. Instead, the

¹⁴² Ben Comer, *U.S. v. Caronia: What Constitutes 'Truthful' Speech?*, PHARMECEBLOG (Dec. 5, 2012), <http://blog.pharmexec.com/2012/12/05/us-v-caronia-what-constitutes-truthful-speech>, archived at <http://perma.cc/WGL2-VWYP> (quoting a former FDA attorney's opinion that “[*Caronia*] switches the burden of proof, so that FDA has to show that something is false or misleading rather than simply off-label”); John Kamp, *Off-Label on the Table*, MED. MARKETING & MEDIA (May 1, 2013), <http://www.mmm-online.com/off-label-on-the-table/article/290961>, archived at <http://perma.cc/7SZF-F9LC> (“The burden of proof should be on the government under this standard. In other words, FDA will have to prove something is false or misleading . . .”).

¹⁴³ See *Pearson v. Shalala*, 164 F.3d 650, 658 (D.C. Cir. 1999).

¹⁴⁴ See Rankin, *supra* note 2.

argument is focused on the particular circumstances of off-label promotion: a nonmedia defendant, engaging in self-interested commercial speech about a product that it has declined the option of proving to FDA the efficacy and safety for the indication suggested, where talk is cheap since efficacy and safety cannot be known through accumulation of anecdotes alone, in a domain where the costs of falsehood can be life-or-death for patients that forgo other treatments and suffer side effects, and where the actual crime alleged regulates behavior (the introduction of a drug in interstate commerce), rather than speech in the first place.¹⁴⁵ If the First Amendment has vitality in this domain at all, then it will permit the courts to purport to be as ignorant as they really are about the multitude of potential claims to drugs' safety and efficacy. The First Amendment will protect truthful speech where we can say with some warrant that the label applies.

Once shown in this light, it becomes clear that the current FDCA regulatory regime *already* provides a constitutional framework for truthful promotion of drugs. To avoid prosecution for misbranding its products, the manufacturer may spend the time and money to prove to FDA the truth of its promotional claims. In this sense, the FDCA provides the very procedure for testing and redeeming the First Amendment's protections for truthful commercial speech. Courts have recognized as much.¹⁴⁶ The advantage of using this procedure, which Congress enacted, is that FDA has the institutional capacity to provide a robust and scientifically rigorous assessment of the drugmaker's promotional claims.¹⁴⁷ Because the FDA-approval regime provides an avenue for truthful

¹⁴⁵ In *United States v. Alvarez*, the Court invoked such pragmatic considerations when it underscored the constitutionality of perjury statutes, both state and federal, saying that "[i]t is not simply because perjured statements are false that they lack First Amendment protection. Perjured testimony 'is at war with justice' because it can cause a court to render a 'judgment not resting on truth.'" 132 S. Ct. 2537, 2546 (2012) (plurality opinion) (quoting *In re Michael*, 326 U.S. 224, 227 (1945)). Much the same can be said for a false statement about a drug's safety and efficacy; the falsehood is at war with *health* because it can cause a *doctor* to render a *prescription* not resting on truth.

¹⁴⁶ *Nutritional Health Alliance v. Shalala*, 144 F.3d 220, 228 (2d Cir. 1998) ("[I]t is significant that the speech involved is indisputably 'pure commercial' speech, and that the regulation pertains to health and safety. . . . [G]iven the need to protect consumers before any harm occurs, we conclude that the 540-day prior restraint is sufficiently narrowly tailored. It grants a limited, but reasonable, time within which the FDA can evaluate the evidence in support of labeling claims. And it allows for the development of a record on the matter so that a court can determine whether the regulated speech is, in fact, truthful and non-misleading, as is required by the first prong of the Central Hudson test.").

¹⁴⁷ See 21 U.S.C. § 355 (2012) (setting standards for scientific proof in the premarket approval process); *Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 844 (1984) ("We have long recognized that considerable weight should be accorded to an executive department's construction of a statutory scheme it is entrusted to administer, and the principle of deference to administrative interpretations." (citation omitted)); *Steadman v. SEC*, 450 U.S. 91, 95-96 (1981) ("Where Congress has not prescribed the degree of proof which must be adduced by the proponent of a rule or order to carry its burden of persuasion

speech, prosecution for off-label promotion would thus raise no constitutional problem.

If the courts nonetheless refuse to defer conclusively to the epistemic test established by the co-equal branches, the courts still need not adopt judicial naiveté, presuming the truth of off-label promotional claims. When a drugmaker refuses or fails to prove a promotional claim to FDA, and then faces enforcement for selling a misbranded product in interstate commerce, the courts should, at the very least, impose on drugmakers the burden of proving their promotional claims true as an affirmative defense at a jury trial. This alternative framework, then, gives the drugmakers two chances to prove truth (first in the FDA safe harbor, and second at trial), without going so far as to presume whatever they say is true.¹⁴⁸

Under such a regime, the courts will presumably use their own established authority to regulate scientific speech in the courtroom. Thus, the manufacturer will contemplate the difficulty of actually proving the truth of its off-label promotional claims in a court of law, controlled by the Rules of Evidence and the limits on the admissibility of expert testimony and scientific evidence.¹⁴⁹ The courts may not require the rigorous randomized controlled trials contemplated in the FDCA, but they will require something more than the ipse dixit of the sales representative, or even the educated guesses of physicians. Thus, given the huge stakes of a criminal conviction, the manufacturer's opportunity to prove the affirmative defense that the promotional claims were true may actually provide little succor to defendants who lack rigorous scientific support for their claims.

One might worry that the courts are less competent to resolve these specialized technical questions. That is why we have FDA in the first place. Still, such a fallback reconceptualization of the premarket approval process as a safe harbor is better than the current regime of judicial naiveté.

Without some sort of reconstruction of FDA regulation of off-label promotion, the Supreme Court's expansive First Amendment doctrine threatens to return us to a pre-FDCA world where drugs are presumed to cure any disease that the drugmakers say they cure, at least until somebody proves them false. Especially in contexts where information is expensive, the speaker is in the best position to purchase that information, and because the stakes are high, the First Amendment should not proceed on bald presumptions about the truth.

in an administrative proceeding, this Court has felt at liberty to prescribe the standard, for '[i]t is the kind of question which has traditionally been left to the judiciary to resolve.' However, where Congress has spoken, we have deferred to 'the traditional powers of Congress . . .'" (quoting *Woodby v. INS*, 385 U.S. 276, 284 (1966)).

¹⁴⁸ FDA asserted such a "safe harbor" theory in its defense of its off-label promotions regulation in the case of *Washington Legal Foundation v. Henney*, 202 F.3d 331, 335-36 (D.C. Cir. 2000). See Conko, *supra* note 4, at 169.

¹⁴⁹ See *supra* notes 115-19 and accompanying text.