United States Court of Appeals

for the

First Circuit

Case No. 21-1080

UNITED STATES,

Appellee,

– v. –

WILLIAM FACTEAU,

Defendant-Appellant.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF MASSACHUSETTS, NO. 1:15-CR-10076

BRIEF OF WASHINGTON LEGAL FOUNDATION AS *AMICUS CURIAE* IN SUPPORT OF DEFENDANT-APPELLANT AND REVERSAL

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Regulations

Statutes

Other Authorities

INTERESTS OF *AMICUS CURIAE*[1]

Washington Legal Foundation (WLF) is a nonprofit, public-interest law firm and policy center with supporters nationwide. WLF promotes free enterprise, individual rights, limited government, and the rule of law. It often appears as an *amicus* in cases raising First Amendment issues. *See, e.g.*, *Sorrell* v. *IMS Health Inc.*, 564 U.S. 552 (2011); *Nike* v. *Kasky*, 539 U.S. 654 (2003). WLF has successfully challenged the constitutionality of Food and Drug Administration (FDA) restrictions on speech by pharmaceutical manufacturers. *Washington Legal Found.* v. *Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998), *appeal dismissed*, 202 F.3d 331 (D.C. Cir. 2000). As a result of that litigation, FDA is subject to a permanent injunction limiting its authority to suppress manufacturers' dissemination of certain journal articles/medical texts discussing off-label uses of their FDA-approved products.

WLF also played a key role in overturning — on First Amendment grounds — the criminal conviction of a pharmaceutical representative for

[1] No party's counsel authored any part of this brief. No one, apart from WLF and its counsel, contributed money to fund the brief's preparation or submission. All parties have consented to the brief's being filed.

conspiring to violate the Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. §§ 301 *et seq.*; the defendant's 'crime' consisted of speaking truthfully about off-label uses of a drug manufactured by his company. *United States* v. *Caronia*, 703 F.3d 149 (2d Cir. 2012). And WLF filed an *amicus* brief in a key case that enjoined the FDA from restricting a pharmaceutical company's constitutionally protected speech. *Amarin Pharma, Inc.* v. *United States FDA*, 119 F. Supp. 3d 196 (S.D.N.Y. 2015).

WLF believes that healthcare improves when doctors have unrestricted access to truthful information about the safety and effectiveness of FDA-approved drugs and medical devices. WLF is concerned that FDA restrictions on truthful speech are denying doctors access to the best available information about FDA-approved drugs and medical devices, thereby interfering with delivery of state-of-the art medical care.

INTRODUCTION

This case is the latest in a long line of cases impermissibly applying FDA regulations to criminalize truthful, non-misleading pharmaceutical speech protected by the First Amendment.[2] First were the WLF cases of the late-1990s, in which courts struck down FDA guidance restricting the dissemination of truthful and non-misleading scientific publications to medical professionals. *See Friedman*, 13 F. Supp. 2d 51.

Then, in 2011, came the Supreme Court's monumental holding in *Sorrell*, in which the Court struck down a Vermont law restricting pharmacies and pharmaceutical manufacturers from disclosing, or otherwise using for marketing purposes, pharmacy records revealing doctors' prescribing practices. 564 U.S. 552. In so doing, the Supreme Court held that "[s]peech in aid of pharmaceutical marketing . . . is a form of expression protected by the Free Speech Clause of the First Amendment." *Id.* at 557.

[2] Although this brief is filed only in *United States* v. *Facteau*, 21-1080, the arguments herein apply with equal force to *United States* v. *Fabian*, 21-1082.

One year later, the Second Circuit vacated Alfred Caronia's conviction for misbranding the drug Xyrem in violation of 21 U.S.C. §§ 331(a) and 333(a)(1). *Caronia*, 703 F.3d 149. Because Caronia's conduct amounted to no more than truthfully and non-misleadingly promoting the drug for an off-label use,[3] and because off-label promotion is constitutionally-protected "[s]peech in aid of pharmaceutical marketing," *id.* at 162, Caronia's conviction could not stand.

Caronia's holding was reaffirmed three years later, in 2015, when the FDA was enjoined from prohibiting Amarin Pharma from engaging in truthful, non-misleading off-label promotion of the drug Vascepa. *Amarin*, 119 F. Supp. 3d 196. The *Amarin* court left no doubt about *Caronia*'s wide-ranging application:

> "The Second Circuit's thoroughgoing First Amendment analysis in *Caronia*, which led it to construe the FDCA's misbranding provisions so as not to reach truthful speech promoting off-label use, further ***defeats the FDA's attempt to marginalize the holding in that case as fact-bound***." *Id.* at 225 (emphasis added).

[3] An "off-label use" refers to a use of a pharmaceutical in a manner not specified in the FDA's approved packaging, packaging label, or insert. It is perfectly legal and common.

The FDA's most recent attempt to criminalize truthful, non-misleading speech through its misbranding regulations was thwarted by a 2016 jury acquittal in the Western District of Texas. *See* Jury Verdict (ECF No. 286), *United States* v. *Vascular Solutions, Inc.*, 5:14-cr-926-RCL (W.D. Tex. Feb. 26, 2016). In *Vascular Solutions*, the jury was properly instructed that if it found that the defendants' "promotional speech to doctors was solely truthful and not misleading, then [it] must find the Defendants not guilty of the misbranding offense." Jury Instrs. (ECF No. 282) at 12, *id.* (W.D. Tex. Feb. 25, 2016).[4]

This case is merely the latest in this unfortunate progeny. To get around *Caronia's* prohibition on the government's ability to prosecute truthful, non-misleading off-label promotion as a crime itself, the FDA has latched on to the *Caronia* court having left open the possibility that truthful, non-misleading speech could be used as evidence of intended use — though it acknowledged it "remains unclear" how the government would be able to do so. 703 F.3d at 162 n.9. The government's attempt

[4] It was error for the jury in this case not to be similarly instructed.

to shoehorn its case here into that exception proves that it has still not figured out how to do so consistent with the First Amendment.

To make its case, the government relied heavily on Defendants' efforts to engage in truthful, non-misleading off-label promotion. Without that evidence, the government's case collapses. The FDA is, therefore, in effect still attempting to criminalize protected speech.

The FDA's misbranding and adulteration regulations may not, consistent with the First Amendment, criminalize off-label promotion where, as here, it comprises truthful, non-misleading speech. Notwithstanding the portrayal of truthful, non-misleading off-label promotion as "merely" evidence of the intent to commit a crime, rather than the crime itself, the constitutional infringement remains. Such application of the FDA's misbranding and adulteration regulations cannot survive First Amendment scrutiny.

BACKGROUND

I. THE FDA CRIMINALIZES TRUTHFUL, NON-MISLEADING OFF-LABEL PROMOTION.

The FDA does not regulate the practice of medicine, so once a drug or medical device is approved by the FDA for any indication, it is perfectly

legal for doctors to prescribe medicines or use medical devices for "off label" uses — i.e., uses not approved by the FDA. And no federal statute prohibits drug or device manufacturers from engaging in off-label marketing or promotion. The FDA, however, criminalizes such conduct by "patching together" the FDCA's misbranding and adulteration regulations in a way that, in the FDA's view, criminalizes *all* off-label promotion, even if it is truthful and non-misleading. *See* Mem. and Order Den. Mot. for J. of Acquittal, or Alternatively, a New Trial (ECF No. 516) at 1.

By consistently basing misbranding and adulteration prosecutions on truthful, non-misleading off-label promotion, the FDA "*criminaliz[es] conduct that it is not entirely clear Congress intended to criminalize*." *See id.* (emphasis added); *Caronia*, 703 F.3d at 169 ("[T]he government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label use of an FDA-approved drug."); *Amarin*, 119 F. Supp. 3d at 237 ("Amarin may engage in truthful and non-misleading speech promoting the off-label use of Vascepa . . . such speech may not form the basis of a prosecution for misbranding.").

The FDCA prohibits the "adulteration or misbranding of any food, drug, device, tobacco product, or cosmetic in interstate commerce." 21 U.S.C. § 331. A drug or device is adulterated and misbranded when the product moves in interstate commerce without FDA approval. 21 U.S.C. §§ 351(f)(1)(B) (adulteration), 352(o) (misbranding). The FDA reads these provisions too broadly, deeming drugs and devices adulterated and misbranded if a manufacturer's speech about them, at any time following FDA approval, promotes a use not included in the FDA-approved labeling. The FDA now considers such speech, notwithstanding its truthful, non-misleading nature, as evidence of "intended use" under 21 C.F.R. § 801.4, upon which misbranding and adulteration liability hinges.

In reality, off-label use is a widespread "accepted medical practice." AHFS, Drug Information xiv (2012). In fact, (i) 21% of *all* prescriptions, *see* David C. Radley, et al., *Off-label Prescribing Among Office-Based Physicians*, 166 Archives Internal Med. 1021, 1021 (2006); (ii) 80% of pediatric prescriptions, U.S. Gen. Accounting Office, GAO/T-HEHS-96-212, *Prescription Drugs: Implications of Drug Labeling and Off-Label Use* 3 n.6 (1996); (iii) 96% of pediatric intensive care unit prescriptions, *Off-*

Label Medications Prescribed to Nearly All Pediatric Intensive Care Patients, American Academy of Pediatrics (Oct. 21, 2012); (iv) between 19% and 43% of adult critical care patient antibiotic prescriptions, G.S. Tansarli, et al., *Frequency of the off-label use of antibiotics in clinical practice: a systematic review*, 10(2) Expert Rev. Anti-infective Therapy 1383 (2012); and (v) at least 50% of oncology prescriptions, Paolo G. Casali, Editorial, *The Off-Label Use of Drugs in Oncology: A Position Paper by the European Society for Medical Oncology (ESMO)*, 18 Annals Oncology 1923, 1923 (2007), are for off-label uses. The FDA itself even "contemplates that approved drugs will be used in off-label ways." *Caronia*, 703 F.3d at 166.

In certain medical fields, such as oncology and pediatrics, "patient care *could not proceed* without off-label prescribing." Rebecca Dresser & Joel Frader, *Off-Label Prescribing: A Call for Heightened Professional and Governmental Oversight*, 37(3) J.L. Med. & Ethics 476 (2009) (emphasis added). This is because it is particularly difficult to conduct the clinical trials necessary to obtain drug approval with children, and cancer patients are often unable to survive the multi-year clinical-trial process required to secure supplemental FDA approval for a new use.

"[O]ff-label uses or treatment regimens," therefore, "may even constitute a medically recognized standard of care." *Caronia*, 703 F.3d at 153 (quoting U.S. Food and Drug Administration, *Draft Guidance, 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* 3 (2009) (internal quotation marks omitted)); *see also* Nat'l Insts. of Health, Nat'l Cancer Inst., *Off-Label Drug Use in Cancer Treatment* (Jan. 1, 2014) ("Often, usual care for a specific type or stage of cancer includes the off-label use of one or more drugs.").

Federal law not only permits off-label use, it subsidizes it. Medicare and Medicaid, for instance, must reimburse for certain off-label uses included in medical compendia. *See* 42 U.S.C. §§ 1395y(a)(1)(A), 1396r-8(k)(6); Medicare Benefit Policy Manual, Ch. 15 § 50.4.2.

Under FDA's construct of the FDCA, only pharmaceutical manufacturers are prohibited from promoting the off-label use of a drug or device. Off-label promotion by other categories of speakers, such as physicians and academics, will not constitute evidence of a new intended use for the drug or device. They may therefore "speak about off-label use

without consequence." *Caronia*, 703 F.3d at 165 (citing 21 U.S.C. §§ 331(a), 333(a)).

By prohibiting off-label promotion while permitting off-label use, the FDA "paternalistically" interferes with the ability of physicians and patients to receive relevant treatment information. *Caronia*, 703 F.3d at 166 (citing *Va. Bd. of Pharmacy* v. *Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 770 (1976); *Sorrell*, 564 U.S. at 575-80)). The government's construction of the FDCA essentially legalizes the outcome (off-label use), while prohibiting the "free flow of information that would inform that outcome." *Id.* at 167.

Under the current FDCA regime, pharmaceutical manufacturers may not convey, without fear of criminal penalty, truthful, non-misleading information to doctors about off-label use. Any off-label promotion will constitute evidence of a new "intended use" and will lead to the drug or device being misbranded and adulterated because information about that use is not included in the FDA-approved label.

This regime — as applied here — cannot withstand First Amendment scrutiny.

II. DEFENDANTS' AND ACCLARENT'S PROMOTION OF STRATUS'S OFF-LABEL USE WAS TRUTHFUL AND NON-MISLEADING SPEECH.

Acclarent, founded in 2004, is a medical equipment manufacturing company focused on helping people breathe without surgery. *See* JA.1230:3-20. Facteau was Acclarent's CEO from November 2004 through December 2011, JA.1228:22-23; JA.2037:17-18, and Fabian was Acclarent's VP of Sales from August 2007 through November 2011, JA.1393:10-12; JA.2037:19-20. Acclarent created a medical device called the Stratus MicroFlow Spacer (Stratus). The device is inserted into a person's sinus and releases an agent to relieve pain by treating chronic ethmoid mucosal disease. *See* Peter J. Catalano, et al., *The MicroFlow Spacer: A Drug-Eluting Stent for the Ethmoid Sinus*, 63(3) Indian J. Otolaryngology Head & Neck Surgery 279 (2011).

In September 2006, the FDA approved Stratus for use as a postoperative spacer to maintain an opening to the ethmoid sinus within the first fourteen days following surgery. JA.4732; JA.4724-4726; JA.4751; JA.1823.

In April 2007, Acclarent sought FDA approval of Stratus for use with the delivery of drugs. JA.1468:2–15; JA.1500:16–22. The FDA

denied Acclarent's request to expand Stratus's indication to include drug delivery, finding that additional information was required. JA.1501:21-24; JA.1828:3–5.

Most physicians who used Stratus did so for an off-label use — with Kenalog-40 (a steroid used to treat inflammation) — as they are legally permitted to do. JA.1861:2-14. Stratus solved the challenge of delivering Kenalog-40 into the sinuses by permitting delivery into difficult-to-reach sinus areas. JA.1503:10-15. Doctors used the device to deliver Kenalog-40 directly into a person's nasal tissue to help treat chronic sinusitis, a chronic inflammatory disease, while avoiding side effects of administering the drug systemically. JA.1941:12-18; *see also* JA.1517:11-14; JA.2224:3-10.

Given how Stratus was actually used, Defendants and Acclarent employees marketed and promoted Stratus's off-label use with truthful and non-misleading speech. At forums, conferences, and directly to doctors, they showed how Stratus could be used beneficially for patients with Kenalog-40. Acclarent's promotional materials and procedures, which the company's regulatory department approved as FDCA-compliant, were predicated on FDA guidelines providing "safe harbors"

for permissible communications regarding off-label uses with physicians. *See* JA.199-210; JA.3902-3906; *see also* JA.1321A-B; 1347A-C; 1354A-B; JA.2793-2798; JA.2824-2828; JA.4621-4629.

III. THE FDA PROSECUTES DEFENDANTS FOR TRUTHFUL AND NON-MISLEADING SPEECH PROMOTING STRATUS'S OFF-LABEL USE.

Defendants Facteau and Fabian were indicted for: (i) five counts of introducing a misbranded device into interstate commerce, in violation of 21 U.S.C. §§ 331(a), 333(a)(1)-(2), 352(a), 352(f), 352(o)[5]; (ii) five counts of distributing an adulterated device into interstate commerce, in violation of 21 U.S.C. §§ 331(a), 333(a)(1)-(2), 351(f)(1)(B)[6]; (iii) one count of conspiring to commit adulteration and misbranding, in violation of 18 U.S.C. § 371; (iv) four counts of wire fraud and attempted wire fraud, in violation of 18 U.S.C. §§ 1343, 1349; and (v) three counts of securities

[5] Defendants were charged under three distinct misbranding theories: (i) that the device's labeling was false and misleading, in violation of 21 U.S.C. § 352(a); (ii) that the device lacked adequate directions for use, in violation of 21 U.S.C. § 352(f); and (iii) that no pre-market notification was provided for the device as required by Section 510(k), in violation of 21 U.S.C. § 352(o).

[6] Defendants were charged with adulteration in that the device lacked an FDA pre-market approval and was not properly exempt from such approval, in violation of 21 U.S.C. § 351(f)(1)(B).

fraud, in violation of 15 U.S.C. §§ 78j(b), 78ff(a), and 17 C.F.R. § 240.10b-5. JA.0030-0062. Defendants were charged with misbranding and adulteration in both felony and misdemeanor form, the former requiring the Government to demonstrate that the violations were committed with the intent to defraud or mislead. *See* 21 U.S.C. § 333(b). Shortly before trial, the Government dismissed the three securities fraud counts and one wire fraud count relating to the alleged securities fraud. JA.0380-0381.

During a 27-day trial, the evidence demonstrated that Defendants did no more than truthfully and non-misleadingly promote Stratus for its off-label use of delivering Kenalog-40. For example, key materials that Acclarent employees used to promote Stratus, including a Physician Discussion Guide and a "Pre-Call" sales talking points outline, discussed using the Stratus with Kenalog-40. JA.2796; JA.4263. These promotional efforts were overseen and approved as FDA-complaint by Acclarent's regulatory department. Acclarent policy was to comply with FDA's safe harbors.

Nevertheless, at trial, the government focused principally on Defendants' efforts to promote the off-label use of Stratus, which was how

doctors primarily prescribed the device, using truthful, non-misleading speech. And the jury convicted Defendants by using that protected speech as the basis for of their supposed crimes.

Significantly, the jury rejected the argument that the speech at issue here was false or misleading. The verdict form's special interrogatories asked the jury to indicate whether it based its misdemeanor misbranding conviction on a theory of (i) false and misleading labeling or (ii) lack of adequate directions for use, and the jury expressly rejected both of those theories. JA.0460-1469.[7] Defendants' acquittal on the charge of false or misleading labeling highlights the jury's conclusion that their promotional efforts were entirely truthful and non-misleading.[8]

While the District Judge instructed the jury that "truthful, non-misleading speech alone cannot be the basis for a criminal conviction,"

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[7] The verdict form made clear that the conviction was based solely on a pre-market notification theory, which is not based on the false or misleading nature of the speech involved. JA.0460-0469.

[8] That the verdict form did not similarly contain special interrogatories for the adulteration charges, showing acquittal for false or misleading labeling, is inconsequential because the adulteration and misbranding charges were based on the same evidence.

Jury Instrs. (ECF No. 436) at 27, this was insufficient because it was not made clear to the jury what other actions would permit a conviction. For example, if the jury were to conclude — as they could have based on the jury instructions here — that a conviction could be based solely on truthful and non-misleading speech and the introduction of a medical device into interstate commerce, that would have been insufficient to survive First Amendment scrutiny. *See Caronia*, 703 F.3d at 168 ("We construe the misbranding provisions of the FDCA as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs."). Likewise, if the jury were to have convicted based solely on truthful and misleading speech and the Defendants' physical attendance at sales meetings or conferences where sales of the Acclarant was discussed, that too would fail to satisfy the First Amendment. *Id.*

Under recent precedent, the jury instruction was inadequate. To satisfy the First Amendment, the jury should have been instructed (as requested by Defendants) that, if Defendants' "promotional speech to doctors was solely truthful and not misleading, then [it] ***must*** find the Defendants not guilty of the misbranding offense." *See* Jury Instrs. at 12, *Vascular Solutions, Inc.*, 5:14-cr-926-RCL (emphasis added). So

Defendants most likely were convicted for no more than their truthful, non-misleading off-label promotion and marketing of Stratus. Under well-established First Amendment law, their convictions may not stand.

ARGUMENT

I. APPLYING THE MISBRANDING AND ADULTERATION REGULATIONS TO CRIMINALIZE DEFENDANTS' TRUTHFUL, NON-MISLEADING SPEECH VIOLATES THE FIRST AMENDMENT.

The misbranding and adulteration regulations as applied here are content-, viewpoint-, and speaker-based restrictions on speech, and do not withstand First Amendment scrutiny.

A. The FDCA Misbranding And Adulteration Regulations As Applied Warrant Strict Scrutiny Because They Are Content-, Viewpoint-, And Speaker-Based Restrictions On Speech.

As applied by the FDA, the misbranding and adulteration regulations target "[s]peech in aid of pharmaceutical marketing," which is a "form of expression protected by the Free Speech Clause of the First Amendment." *Sorrell*, 564 U.S. at 557. That the FDA argues that the truthful, non-misleading speech is "merely" evidence of intended use (upon which liability under these statutes hinges), does not change this

when, as here, the evidence focuses principally on truthful and non-misleading off-label promotion.

The government here is still regulating speech because it disagrees with that speech's message and, therefore, "heightened scrutiny" applies. *Sorrell*, 564 U.S. at 566; *see also Caronia*, 703 F.3d at 164-65 ("The government's construction of the FDCA's misbranding provisions to prohibit and criminalize the promotion of off-label drug use by pharmaceutical manufacturers is content- and speaker-based, and, therefore, subject to heightened scrutiny.").

The FDA's construction of the misbranding and adulteration regulations specifically "disfavor[] [off-label] *marketing*," that is, "speech with a particular *content*," *Sorrell*, 564 U.S. at 564 (emphasis added). The regulations, as applied here, are, therefore, "content-based restrictions on speech . . . [and] can stand only if they survive strict scrutiny[.]" *Reed* v. *Town of Gilbert*, 576 U.S. 155, 171 (2015); *see also Nat'l Inst. of Family & Life Advocates* v. *Becerra*, 138 S. Ct. 2361, 2371-72 (2018) ("*NIFLA*") (applying strict scrutiny to content-based regulation). Content-based laws, which "target speech based on [their] communicative content . . . are presumptively unconstitutional and may be justified only if the

government proves they are narrowly tailored to serve compelling state interests." *Reed*, 576 U.S. at 163 (citing *R.A.V.* v. *St. Paul*, 505 U.S. 377, 395 (1992)); *see also Sorrell*, 564 U.S. at 566 (expressing particular concern over content-based restrictions "in the fields of medicine and public health, where information can save lives").

These regulations, as applied here, are a particularly "egregious form of content discrimination" because they discriminate "among *viewpoints* . . . speech based on the specific motivating ideology or opinion or perspective of the speaker." *Reed*, 576 U.S. at 168-69 (quoting *Rosenberger* v. *Rector and Visitors of Univ. of Va.*, 515 U.S. 819, 829 (1995) (internal quotation marks omitted) (emphasis added)). As applied here, the misbranding and adulteration provisions prohibit only *positive* characterizations of off-label use, while permitting speech *discouraging* off-label use. Such viewpoint discrimination is all the more harmful because "off-label uses or treatment regimens . . . may even constitute a medically recognized standard of care." *Caronia*, 703 F.3d at 153 (quoting U.S. Food and Drug Administration, *Draft Guidance*, *supra*, at 3 (internal quotation marks omitted)). Strict scrutiny applies to laws that discriminate against certain viewpoints, which the Supreme Court

has described as "particularly pernicious" and as "censorship in its purest form" because "such regulation often indicates a legislative effort to skew public debate on an issue." *R.A.V.*, 505 U.S. at 430 (Stevens, J., concurring) (internal citation and quotations omitted).

The misbranding and adulteration regulations as applied are also speaker-based speech restrictions because they specifically prevent pharmaceutical manufacturers and their employees — and no one else — from engaging in protected speech. *See Sorrell*, 564 U.S. at 563-65; *Caronia*, 703 F.3d at 165 (finding the government's construction of the FDCA "speaker-based because it targets one kind of speaker — pharmaceutical manufacturers — while allowing others to speak without restriction"). Other categories of speakers, meanwhile, such as physicians and academics, are free to "speak about off-label use without consequence." *Id.* (citing 21 U.S.C. §§ 331(a), 333(a)). When a regulation is both speaker-based *and* content- or viewpoint-based, the need for "heightened scrutiny" is overwhelming. *See Sorrell*, 564 U.S. at 563-66. That is particularly true "in the fields of medicine and public health, where information can save lives." *Id.* at 566.

B. The FDCA Misbranding And Adulteration Regulations As Applied Fail Strict Scrutiny Because They Are Not Narrowly Tailored to Serve a Compelling Government Interest.

The misbranding and adulteration regulations as applied fail strict scrutiny because the Government cannot prove that "they are narrowly tailored to serve compelling state interests." *Reed*, 576 U.S. at 163 (citing *R.A.V.*, 505 U.S. at 395). Even if the Government's interest in "protecting and promoting the public health"[9] were sufficiently compelling, the regulations as applied are not narrowly tailored to achieve that interest because less speech-restrictive alternatives and non-criminal penalties are available. *See Caronia*, 703 F.3d at 167 (citing *Thompson* v. *W. States Med. Ctr.*, 535 U.S. 357, 372-73 (2002)); *see also Sable Commc'ns of Cal., Inc.*, v. *F.C.C.*, 492 U.S. 115, 126 (1989) ("The Government may . . . regulate the content of constitutionally protected speech in order to promote a compelling interest *if it chooses the least restrictive means to further the articulated interest*.") (emphasis added).

[9] Gov. Opp'n to Defs.' Mot. for J. of Acquittal or, Alternatively, a New Trial (ECF No. 497) at 15.

For instance, the government could: (i) "guide physicians and patients in differentiating between misleading and false promotion, exaggerations and embellishments, and truthful or non-misleading information," *Caronia*, 703 F.3d at 168 (citation omitted); (ii) "develop its warning or disclaimer systems, or develop safety tiers within the off-label market, to distinguish between [devices]," *see id.* (citation omitted); (iii) "further remind physicians and manufacturers of, and even perhaps further regulate, the legal liability surrounding off-label promotion and treatment decisions [i.e., through medical malpractice and negligence]," *id.*; and (iv) "where off-label [device] use is exceptionally concerning, the government could prohibit the off-label use altogether." *Id.* (citing *United States* v. *Bader*, 678 F.3d 858, 873-75 & n.10 (10th Cir. 2012)).

The misbranding and adulteration provisions as applied here do not and cannot withstand strict scrutiny.

C. The Misbranding And Adulteration Regulations As Applied Do Not Withstand Even Intermediate Scrutiny Under *Central Hudson*.

Even if the misbranding and adulteration provisions as applied here need not satisfy strict scrutiny, they would still be subject to the rigorous intermediate scrutiny test in *Central Hudson Gas & Electric*

Corp. v. *Pub. Serv. Comm'n*, 447 U.S. 557 (1980).[10] *See Caronia*, 703 F.3d at 162-69 (applying *Central Hudson* to FDCA misbranding provision before *Reed* and *NIFLA* decisions).

Under *Central Hudson*, speech "concern[ing] lawful activity" that is not misleading is protected, unless the government shows that its restriction on speech serves "a substantial interest," the restriction "directly advance[s] the state interest involved," and the restriction is not "more extensive than necessary to serve that interest." 447 U.S. at 564, 566.

The Defendants' speech cannot form the basis of a criminal conviction under this test. Promoting the off-label use of a medical device concerns lawful activity (off-label medical device use), and the promotion at issue is neither false nor misleading. *See Caronia*, 703 F.3d at 165.[11]

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[10] The *Central Hudson* test has been applied rigorously in recent years. *See, e.g.*, *Matal* v. *Tam*, 137 S. Ct. 1744 (2017).

[11] To lose *Central Hudson* protection, commercial speech must be *inherently*, rather than *potentially*, misleading. *Pearson* v. *Shalala ("Pearson II")*, 130 F. Supp. 2d 105, 113 (D.D.C. 2001) ("If information is 'inherently' misleading, it may be banned entirely. In the case of 'potentially misleading commercial speech,' a court reviewing a challenge to such a government regulation must employ [the *Central Hudson* test].") (internal citations omitted); *accord Friedman*, 13 F. Supp. 2d at

Even if the Government's interest in "protecting and promoting the public health"[12] were sufficiently important to satisfy the second prong, the misbranding and adulteration regulations as applied here still fail because they are not sufficiently tailored to that interest. *See Caronia*, 703 F.3d at 166-69 (finding that FDCA's prohibition of off-label promotion did not directly advance, and was more extensive than necessary to serve, the government's interest in protecting and promoting public health).

The misbranding and adulteration regulations do not "directly [and materially] advance" the Government's interest in protecting and promoting public health. *Rubin* v. *Coors Brewing Co.*, 514 U.S. 476, 488-89 (1995) (striking down prohibition on display of alcohol content on beer

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66-67. Where, as here, the scientific evidence is at worst inconclusive and is properly disclaimed, related speech does not lose First Amendment protection. *Pearson II*, 130 F. Supp. 2d at 118 ("FDA *may not* ban . . . [a c]laim simply because the scientific literature is inconclusive[.]"); *see Whitaker* v. *Thompson*, 248 F. Supp. 2d 1, 10 (D.D.C. 2002) (citing *Pearson* v. *Shalala ("Pearson I")*, 164 F.3d 650, 659 (D.C. Cir. 1999) (Adding "a clarifying disclaimer to a potentially misleading health claim" provides "the public with information while satisfying the government's concerns about the completeness of the information being provided.")).

[12] Gov. Opp'n to Defs.' Mot. for J. of Acquittal or, Alternatively, a New Trial at 15.

labels under *Central Hudson* test because it did not "directly and materially" advance the government's interest in curbing strength wars among brewers); *Caronia*, 703 F.3d at 166-67. Despite pharmaceutical manufacturers' prohibition from promoting devices off-label, physicians can prescribe, and patients can use, medical devices for off-label purposes. *See id.* at 166. Therefore, prohibiting truthful off-label promotion does not directly and materially reduce patient exposure to unsafe and ineffective devices. *See id.* Prohibiting off-label promotion while simultaneously permitting off-label use "paternalistically" interferes with the ability of physicians and patients to receive relevant and potentially life-saving treatment information; such chilling of information on off-label use could impede, to the public's detriment, informed and intelligent treatment decisions. *Id.* (citing *Va. Bd. of Pharmacy*, 425 U.S. at 770; *Sorrell*, 564 U.S. at 575-80).

Moreover, the regulations are "more extensive than necessary to serve" the Government's interest in protecting and promoting public health. *See Caronia*, 703 F.3d at 167-68. As explained above, various less speech-restrictive alternatives and non-criminal penalties are available. *Id.* at 167 (citing *Thompson*, 535 U.S. at 372-73).

The misbranding and adulteration regulations as applied here target speech protected under *Central Hudson*. Defendants' convictions, therefore, may not stand.

D. The FDCA Misbranding And Adulteration Regulations As Applied Are Void for Vagueness Under the First Amendment.

As applied here, the misbranding and adulteration regulations are void for vagueness because they lack "the precision that the First Amendment requires when a statute regulates the content of speech." *Reno* v. *ACLU*, 521 U.S. 844, 874 (1997). In the context of free speech, because "the standards of permissible statutory vagueness are strict," the "government may regulate in the area only with narrow specificity." *Keyishian* v. *Bd. of Regents of the Univ. of N.Y.*, 385 U.S. 589, 604 (1967) (quoting *N.A.A.C.P.* v. *Button*, 371 U.S. 415, 432-33 (1967)). That is particularly true here because (i) the intended audience consisted of "sophisticated and experienced consumers," such as "prescribing physicians," *Sorrell*, 564 U.S. at 577 (quoting *Edenfield* v. *Fane*, 507 U.S. 761, 775 (1993) (internal quotation marks omitted)); and (ii) the FDCA regulations carry "criminal penalties and fear of incurring these sanctions may deter those who seek to exercise protected First

Amendment rights." *Buckley* v. *Valeo*, 424 U.S. 1, 76-77 (1976) (*per curiam*).

Because it is far from clear what speech the misbranding and adulteration regulations as applied permit, and what speech will result in criminal liability, they lack the precision required of content-based regulations. As Judge Burroughs eloquently described,

> it seems clear that the statutory and regulatory scheme needs to be rethought . . . where a conviction can result in exclusion from healthcare programs, likely a death knell for any company, it is also important for the regulatory and law enforcement regime to clearly spell out what is and is not prohibited conduct.

Mem. and Order Den. Mot. for J. of Acquittal, or Alternatively, a New Trial at 1-2.

The misbranding and adulteration regulations fail this task. For instance, pharmaceutical manufacturers can provide off-label information to doctors if they are responding to "unsolicited requests." *See* Jury Instrs. at 27-28. But until December 2011, when the relevant conduct here occurred, it was impossible to discern what "solicited" meant. The FDA summarized this policy in a 1994 Federal Register notice but never defined or gave examples of what constituted an "unsolicited request," and no case law or warning letters gave any

guidance. *See* Citizen Pet'n Regarding the FDA's Policy on Promotion of Unapproved Uses of Approved Drugs & Devices; Request for Cmts., 59 Fed. Reg. 59,820, 59,823 (Nov. 18, 1994).

II. THE CONVICTIONS MUST BE SET ASIDE BECAUSE THERE IS A SUBSTANTIAL CHANCE THAT THE JURY CONVICTED DEFENDANTS FOR ONLY TRUTHFUL, NON-MISLEADING SPEECH.

Because the jury verdict form did not specify the specific behavior underlying the misbranding and adulteration convictions, this Court cannot assume the jury relied on anything other than truthful, non-misleading speech in convicting Defendants. Where, as here, the verdict

> *may* rest on a ground that is invalid because the theory of conviction is contrary to law—as opposed to a ground that is invalid because the evidence supporting it is insufficient as a matter of law—the verdict must be set aside despite the existence of an alternate, legally valid ground of conviction.

United States v. *Richardson*, 421 F.3d 17, 31 (1st Cir. 2005) (citing *Griffin* v. *United States*, 502 U.S. 46, 59 (1991) (emphasis added)); *see also Griffin*, 502 U.S. at 59 (When "jurors [are] left the option of relying upon a legally inadequate theory, there is no reason to think that their own intelligence and expertise will save them from that error").

In *Richardson*, the defendant was convicted of perjury, and the verdict form did not require the jury to specify the statement(s) upon which it convicted. 421 F.3d at 31. The defendant argued that the verdict must be set aside because at least one of the nineteen statements at issue was legally deficient to constitute perjury because they were true or in response to ambiguous questioning. *Id.* Although the court affirmed the conviction following a thorough analysis of each statement, finding each legally sufficient to constitute perjury, it emphasized that it would have reversed if *any* of the statements were either true or made in response to ambiguous questioning. *Id.*

As noted above, the evidence at trial focused principally on Defendants' truthful and non-misleading off-label promotion of an approved medical device. Because it was possible for the jury to have convicted Defendants based on their truthful, non-misleading speech in contravention of the First Amendment, the convictions may not stand.

* * *

Defendants' convictions are but the latest attempt by the FDA to criminalize, through the misbranding and adulteration regulations, entirely truthful, non-misleading off-label promotion. That the FDA

pursues truthful, non-misleading speech as evidence of intended use, rather than a crime in itself, makes no difference. Physicians routinely use Stratus off-label by using it with Kenalog-40. Rather than encourage an open and free dialogue about whether that is in the best interests of patients by permitting Stratus's manufacturer to provide truthful, non-misleading information about that use, the government has applied the misbranding and adulteration regulations to preclude a medical device manufacturer from making its voice heard in the debate. And it has done so with one of the most powerful tools available to the government, the criminal law. Prosecuting Defendants for truthful, non-misleading off-label promotion warrants strict scrutiny under the First Amendment, which the regulations as applied do not and cannot withstand. Defendants' convictions must therefore be set aside.

CONCLUSION

The Court should vacate Defendants' convictions and remand for a judgment of acquittal.

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CERTIFICATE OF COMPLIANCE

I, Joel Kurtzberg, certify:

(i) That this brief complies with the page limit set forth in Circuit Rule 29-2(c)(2). The brief contains 5672 words.

(ii) That this brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6), because it has been prepared using Microsoft Office Word 2016 and is set in 14-point Century Schoolbook font.

July 28, 2021

/s/ Joel Kurtzberg

CERTIFICATE OF SERVICE

I certify that on July 28, 2021, I filed the foregoing brief of Washington Legal Foundation via the CM/ECF system and served the foregoing via the CM/ECF system on all counsel who are registered CM/ECF users.

/s/ Joel Kurtzberg