No. 21-1082

IN THE UNITED STATES COURT OF APPEALS
FOR THE FIRST CIRCUIT

UNITED STATES,

Appellee,

v.

PATRICK FABIAN,

Defendant-Appellant.

On Appeal from the United States District Court for the District of Massachusetts
No. 1:15-cr-10076 (Hon. Allison D. Burroughs)

BRIEF OF PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AND CHAMBER OF COMMERCE OF THE UNITED STATES OF AMERICA AS AMICI CURIAE IN SUPPORT OF DEFENDANT-APPELLANT AND REVERSAL

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CORPORATE DISCLOSURE STATEMENT

Amicus curiae Pharmaceutical Research and Manufacturers of America has no parent corporation and no publicly held corporation owns 10 percent or more of its stock.

Amicus curiae the Chamber of Commerce of the United States of America states that it is a non-profit, tax-exempt organization incorporated in the District of Columbia. The Chamber has no parent corporation, and no publicly held company has 10 percent or greater ownership in the Chamber.

/s/ Jeffrey L. Handwerker___
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INTEREST OF AMICI CURIAE[1]

Pharmaceutical Research and Manufacturers of America (PhRMA) is a voluntary, non-profit association representing the nation's leading biopharmaceutical and biotechnology companies. PhRMA's members are dedicated to discovering medicines that help patients lead longer, healthier, and more productive lives. Since 2000, PhRMA's members have invested over $1 trillion into discovering and developing new treatments and cures, including $91.1 billion in 2020 alone. *See* PhRMA, *About*, https://www.phrma.org/About. PhRMA's members have led the way in developing new vaccines and treatments for COVID-19, with 43% of COVID-19 clinical trials studying products developed by PhRMA's members. PhRMA, *COVID-19 Treatment Progress* (July 26, 2021), https://phrma.org/Coronavirus/Activity-Tracker.

The Chamber of Commerce of the United States of America is the world's largest business federation. It represents approximately 300,000 direct members and indirectly represents the interests of more than three million companies and professional organizations of every size, in every industry sector, and from every

[1] All parties have consented to the filing of this brief. No party's counsel authored this brief in whole or in part, and no entity or person, other than *amici*, their members, or their counsel, made any monetary contribution intended to fund the preparation or submission of this brief. Neither Johnson & Johnson nor its counsel authored this brief in whole or in part, or made a monetary contribution intended to fund the preparation or submission of this brief.

region of the country. An important function of the Chamber is to represent the interests of its members in matters before Congress, the Executive Branch, and the courts. To that end, the Chamber regularly files amicus briefs in cases raising issues of concern to the nation's business community.

Both amici have substantial interests in ensuring that the courts fully protect businesses' First Amendment rights to share truthful, non-misleading information about their products and services. PhRMA's members research and develop medicines for which they secure FDA approval and then market and sell these medicines, which doctors may also prescribe for additional uses that are not approved by FDA. Its members operate under the same FDA regulations that defendants were convicted of violating. Likewise, the Chamber's members, including members that operate under FDA's regulations, frequently provide consumers with truthful and non-misleading information about their products and services. The district court's decision threatens to erode First Amendment safeguards that, until now, courts have consistently held to protect communications of this nature.

INTRODUCTION AND SUMMARY OF THE ARGUMENT

A foundational tenet of First Amendment jurisprudence is that the government cannot regulate speech "based on the message a speaker conveys." *Barr v. Am. Ass'n of Pol. Consultants, Inc.* (*AAPC*), 140 S. Ct. 2335, 2346 (2020)

(quotation marks omitted). Laws targeting speech "based on its communicative content" are thus "presumptively unconstitutional." *Reed v. Town of Gilbert*, 576 U.S. 155, 163 (2015). The dangers of government content-policing are perhaps most acute "in the fields of medicine and public health, where information can save lives." *Sorrell v. IMS Health Inc.*, 564 U.S. 552, 566 (2011).

These principles prohibit the government from criminalizing truthful, non-misleading speech about pharmaceuticals and medical devices—including about unapproved uses of FDA-approved products. Healthcare professionals lawfully may prescribe products for unapproved purposes, and FDA itself recognizes that unapproved uses of drugs and devices are integral to the practice of medicine and often reflect the standard of patient care. For that reason, the government cannot prohibit manufacturers from speaking truthfully to physicians and other healthcare professionals about unapproved uses of FDA-approved products. Such a prohibition is a paradigmatic content-based restriction. *See United States v. Caronia*, 703 F.3d 149, 164-65 (2d Cir. 2012) (vacating conviction for misbranding); *Amarin Pharma, Inc. v. FDA*, 119 F. Supp. 3d 196, 226 (S.D.N.Y. 2015) (issuing declaration that truthful, non-misleading speech cannot form basis for misbranding action).

The convictions here run afoul of these basic First Amendment principles. The jury concluded that defendants' promotional statements about the FDA-

cleared Stratus device were truthful and non-misleading. But defendants were nonetheless convicted of misbranding and adulteration based exclusively on those truthful and non-misleading promotional statements. And as the courts in *Caronia* and *Amarin* explained, prosecutions that depend on protected speech about unapproved uses violate the First Amendment. Here, the district court identified no evidence other than protected speech that defendants intended the device at issue to be used for an unapproved purpose. Their speech, and their speech alone, transformed the lawful act of distributing the Stratus into unlawful conduct. That violates the First Amendment.

The district court sought to reconcile its decision with First Amendment jurisprudence by characterizing the criminal act as "distribution of a device" rather than communication about unapproved uses. Add.33. But that reconciliation fails: the distribution became illegal only when—and only because—defendants spoke truthfully about it. As the Supreme Court has repeatedly held, if "the conduct triggering coverage under the statute consists of communicating a message," the statute targets speech. *Holder v. Humanitarian Law Project*, 561 U.S. 1, 28 (2010).

Accepting the district court's theory would not only violate the First Amendment; it would create a significant circuit split. In *Caronia*, *Amarin*, and indeed in every single case involving misbranding or adulteration, the

manufacturer has or will have distributed its product in commerce. If the act of distribution nullified First Amendment protections for truthful and non-misleading speech, there would have been no need to vacate the conviction in *Caronia*, and no need for the declaratory relief in *Amarin*.

There is no compelling governmental interest in criminalizing truthful and non-misleading speech about the unapproved uses of FDA-approved medicines and devices. To the contrary, permitting the government to criminalize such speech could gravely harm public health by depriving healthcare professionals of vital information about beneficial, life-saving uses of drugs and devices and by chilling a wide swath of protected speech on important topics. Recognizing that the First Amendment protects truthful and non-misleading speech about unapproved uses would not undermine FDA's robust authority to ensure the safety and effectiveness of drugs and devices it regulates. Although the First Amendment protects truthful, non-misleading speech, the Constitution does not protect false or misleading communications. And manufacturers' communications could be deemed misleading if they omit material information about clinical data supporting the communication. Reversing defendants' convictions therefore would not imperil FDA's efforts to safeguard the public from misinformation in promotional statements. It would simply ensure the continued vitality of critical First

Amendment principles that protect the free flow of truthful, non-misleading information and improve public health.

ARGUMENT

I. Misbranding and Adulteration Prosecutions that Rest on Truthful, Non-Misleading Speech About Off-Label Uses Violate the First Amendment

A. Content-Based Restrictions on Commercial Speech Are Presumptively Unconstitutional

The Supreme Court has made clear that "[s]peech in aid of pharmaceutical marketing" is "a form of expression protected by the Free Speech Clause of the First Amendment." *Sorrell*, 564 U.S. at 557; *see Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 371-77 (2002) (invalidating restrictions on promotion of unapproved compounded drugs). The First Amendment accordingly prohibits the government from targeting truthful and non-misleading pharmaceutical marketing communications on the basis of their content. As the Court explained in *Sorrell*, "[i]n the ordinary case it is all but dispositive to conclude that a law is content based and, in practice, viewpoint discriminatory." 564 U.S. at 571. And that is true, *Sorrell* held, "whether a special commercial speech inquiry or a stricter form of judicial scrutiny is applied." *Id.*

Since *Sorrell*, the Supreme Court has dispelled any doubt that strict scrutiny applies to all content-based speech restrictions, including those governing commercial speech. In *AAPC*, 140 S. Ct. 2335, for example, the Court invalidated

a statutory provision that would have exempted government debt-collection calls from a ban on robocalls. Five Justices concluded that the exemption violated the First Amendment because it was content-based and failed strict scrutiny. *Id.* at 2346-47 (plurality op.); *id.* at 2364 (Gorsuch, J., joined by Thomas, J., concurring in the judgment in relevant part). These five Justices rejected the argument that intermediate scrutiny should apply to content-based restrictions on "commercial speech." *Id.* at 2359 (Breyer, J., dissenting in relevant part). Courts have understood *AAPC* to "repudiat[e] the approach" of applying intermediate scrutiny, rather than strict scrutiny, to content-based commercial-speech restrictions. *Int'l Outdoor, Inc. v. City of Troy*, 974 F.3d 690, 706 (6th Cir. 2020).

It is indisputable that laws relating to speech about unapproved uses of FDA-approved drugs or devices are content-based. As the Supreme Court explained in *Reed*, a law is content-based if it "applies to particular speech because of the topic discussed or the idea or message expressed." 576 U.S. at 163. Indeed, "defin[ing] regulated speech by particular subject matter" constitutes an "obvious," "facial" content-based distinction. *Id.* Accordingly, any statute or regulation that governs speech about the subject matter of unapproved uses is subject to struct scrutiny.

B. The Government Cannot Use Speech as the Trigger to Transform Lawful Conduct into Unlawful Conduct

A second line of Supreme Court jurisprudence governs whether and when a regulation constitutes an impermissible speech restriction, as opposed to a permissible restriction on conduct facilitated by speech. These cases establish that when the government purports to regulate conduct, but the legality of the conduct turns solely on the content of speech, the regulation is functionally a direct regulation of speech and is subject to First Amendment scrutiny.

In *Expressions Hair Design v. Schneiderman*, 137 S. Ct. 1144 (2017), for example, the Supreme Court held that New York's credit card surcharge law was not "simply a conduct regulation," but instead regulated speech. *Id.* at 1150. The law did not prohibit merchants from charging more for credit card transactions; it left them free to set any price they wanted. *Id.* at 1151. Rather, the law regulated "*how* sellers may communicate their prices"—a merchant may charge "$10 for cash and $10.30 for credit," but if so "he must display $10.30 as his sticker price," and "is not free to say '$10, with a 3% credit card surcharge.'" *Id.* (emphasis added). "In regulating the communication of prices rather than prices themselves," the Court held, the law "regulates speech." *Id.* The rule that "a course of conduct" can be illegal even if "the conduct was in part initiated, evidenced, or carried out by means of language" had no relevance. *Id.*; *see AAPC*, 140 S. Ct. at 2347 (plurality op.) ("[l]ike the Vermont law in *Sorrell*," the robocall ban did "not

simply have an effect on speech, but is directed at certain content and is aimed at particular speakers").

Expressions Hair Design thus stands for the critical proposition that the government restricts speech whenever it relies on protected speech as the sole trigger or sole evidence transforming otherwise lawful activity into unlawful activity. As the Eleventh Circuit has put it, applying various Supreme Court precedents: "The State's action is a speech regulation [if] the only difference between the two courses of conduct is the speech." *Ocheesee Creamery LLC v. Putnam*, 851 F.3d 1228, 1237 (11th Cir. 2017) (holding that, because Florida permitted sale of skim milk product without added vitamins, it could not bar seller from calling product skim milk).

The Supreme Court has applied this principle multiple times. For example, though California could undoubtedly prohibit "disturb[ing] the peace [by] offensive conduct" in general, a conviction under that statute was unconstitutional where it "rest[ed] upon" a message worn on the defendant's jacket, and not on any "separately identifiable conduct." *Cohen v. California*, 403 U.S. 15, 16, 18 (1971). Likewise, in *Holder*, the Court applied "demanding" First Amendment scrutiny in evaluating the application of a material-support-for-terrorism law to plaintiffs who wanted to provide legal training—*i.e.*, speak—to covered groups. 561 U.S. at 28. The Court explained that the key question is not whether the law "may be

described as directed at conduct," but whether "the conduct triggering coverage under the statute consists of communicating a message." *Id.*[2]

The Supreme Court has contrasted such speech restrictions with restrictions targeting "commercial activity deemed harmful to the public," where "speech is a component of that activity." *Ohralik v. Ohio State Bar Ass'n*, 436 U.S. 447, 456 (1978). For example, when the government prohibits an "exchange of information about securities" or an "exchange of price and production information among competitors" or "threats of retaliation for the labor activities of employees," it is targeting "illegal conduct" that is in some cases "initiated, evidenced, or carried out by means of language." *Id.*; *see Sorrell*, 564 U.S. at 566-67 (similar). Speech notwithstanding, it is illegal to trade stocks with material nonpublic information, to agree with competitors on price or supply, or to retaliate for labor organizing. Communication is not what *makes* those acts unlawful, *cf. Cohen*, 403 U.S. at 18, but rather the communication is what "carrie[s] out" the independently "harmful" conduct, *Ohralik*, 436 U.S. at 456.

C. FDA Restrictions on Truthful, Non-Misleading Speech About Off-Label Uses Are Unlawful Content-Based Restrictions

Applying these principles, the courts to consider the issue have held that the government cannot impose penalties, much less criminal penalties, on

[2] The Supreme Court ultimately upheld the restriction because it served a compelling interest in combatting terrorism, an interest with no relevance here. *Id.* at 28-39.

manufacturers who engage in truthful, non-misleading speech about the unapproved use of their products. Nor can the government obtain a so-called "misbranding" or "adulteration" conviction where the only difference between the lawful sale of a product and unlawful misbranding or adulteration is truthful, non-misleading speech.

1. The leading case on the constitutionality of these restrictions is the Second Circuit's decision in *Caronia*, which, following *Sorrell*, held that "[t]he 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." 703 F.3d at 164-65. The defendant's conviction failed that scrutiny.

Caronia began with several important, undisputed premises about the promotion of drugs and devices for off-label use and the regulatory framework governing that promotion—the same framework under which defendants were convicted. First, the use of approved drugs for both FDA-approved and FDA-unapproved uses is not only lawful, but critical to patient care in this country. *Id.* at 153. "[O]nce the FDA permits a device to be marketed for one use, health care practitioners have the flexibility to draw on their expertise to prescribe or administer the device for any condition or disease, not just the use the FDA approved—in short, to practice medicine." *Judge Rotenberg Educ. Ctr., Inc. v.*

FDA, ___ F.4th ___, 2021 WL 2799891, at *3 (D.C. Cir. July 6, 2021) (citing 21 U.S.C. § 396). As the "FDA itself has observed," "'unlabeled' 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." *Caronia*, 703 F.3d at 153 (quoting 12 FDA Drug Bull. 1, 5 (1982)).

Recognizing the benefits of responsible off-label use, federal law does not expressly prohibit promotion or marketing of drugs or devices for off-label use. *Id.* at 154. What federal law prohibits instead is "misbranding," which can include, among other things, the failure to obtain premarket clearance for an intended use of a drug or device. *See* 21 U.S.C. § 352(o). Federal law likewise prohibits "adulteration," which includes marketing a medical device requiring premarket approval without obtaining that approval. *Id.* § 351(f)(1)(B). Whether premarket notification or approval is necessary, in turn, depends on whether the manufacturer's "intended use" differs from the use for which the drug or device was previously approved. *See id.* § 360c(i)(1)(A). Federal regulations contemplate that, for both misbranding and adulteration, a manufacturer's "promotion" of a product may, among other things, be evidence of the product's "intended use." *Caronia*, 703 F.3d at 154; *see* 21 C.F.R. § 801.4.

The Second Circuit held that, where truthful and non-misleading promotional speech is the basis for the prosecution, a conviction under this

regulatory scheme violates the First Amendment. The panel rejected the government's argument that the prosecution did not implicate the First Amendment because the defendant's speech was being introduced only "as evidence of intent," not as the criminal "actus reus." 703 F.3d at 160-61 (citing *Wisconsin v. Mitchell*, 508 U.S. 476, 489-90 (1993)). The majority "assume[d], without deciding," *id.* at 162 n.9, that the government could "offer evidence of a defendant's off-label promotion to prove a drug's intended use and, thus, mislabeling for that intended use," *id.* at 161. But, the panel held, truthful and non-misleading promotion could not be the *only* evidence of misbranding—it could not be "determinative of … guilt." *Id.* Not only had the jury instructions in *Caronia* permitted conviction on the basis of promotional speech, but the prosecution also had "never suggested that Caronia engaged in any form of misbranding other than the promotion of the off-label use of an FDA-approved drug"—for example, by "conspir[ing] to place false or deficient labeling on [the] drug." *Id.* "Rather, the record ma[de] clear that the government prosecuted Caronia *for* his promotion and marketing efforts." *Id.*

In other words, the Second Circuit held, because the defendant's conduct would have been lawful but for his truthful, non-misleading speech, the prosecution was the functional equivalent of directly "criminalizing the truthful off-label promotion of FDA-approved" products. *Id.* at 168. And such a

prosecution "unconstitutionally restrict[s] free speech." *Id.* Indeed, *Caronia* held that is true even under intermediate scrutiny, which the court applied because it did not have the benefit of subsequent Supreme Court decisions making clear that strict scrutiny applies to content-based restrictions on commercial speech. *Supra* pp. 6-7. Because "physicians can prescribe, and patients can use," FDA-approved products for unapproved uses, restrictions on speech about those unapproved uses "paternalistically interfere[] with the ability of physicians and patients to receive potentially relevant treatment information" and "could inhibit, to the public's detriment, informed and intelligent treatment decisions." *Id.* at 166 (quotation marks omitted).[3] The government not only "legalizes" but in fact endorses "off-label use" of FDA-approved drugs, and so has no legitimate interest in prohibiting "the free flow of information that would inform that outcome." *Id.* at 167.

2. The second key case is *Amarin*, which held that FDA could not enforce its misbranding authorities based on a manufacturer's promotion of its

[3] *See 44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 503 (1996) (opinion of Stevens, J., joined by Kennedy and Ginsburg, JJ.) ("[B]ans against truthful, non-misleading commercial speech … usually rest solely on the offensive assumption that the public will respond 'irrationally' to the truth. The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good." (cleaned up), *quoted in Thompson*, 535 U.S. at 375); *Va. State Bd. of Pharm. v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 770 (1976) (criticizing government's "highly paternalistic approach" to free flow of truthful, non-misleading information about pharmaceutical products).

drug for off-label use. 119 F. Supp. 3d 196 (S.D.N.Y. 2015). The government sought to characterize *Caronia* as a narrow decision "that turned on the particular jury instructions and government jury addresses given in Caronia's trial." *Id.* at 223-24. The government asserted that, even if the "only acts constituting promotion of [the drug] for an off-label use are [the manufacturer's] truthful and non-misleading statements about that use," the government could permissibly use those statements to "support an inference that [the manufacturer] intended to promote that off-label use." *Id.* at 223. If so, the government theorized, speech would merely be evidence that the manufacturer intended to distribute the drug for an unapproved use—an act independent from the speech itself—and thus the First Amendment would not be implicated.

The court rejected the government's cramped conception of *Caronia*: "Where the speech at issue consists of truthful and non-misleading speech promoting the off-label use of an FDA-approved drug, such speech, under *Caronia*, *cannot* be the act upon which an action for misbranding is based." *Id.* at 226. The government cannot evade this rule by claiming that it not penalizing promotional speech itself, but simply using promotional speech as "evidence of intent" to sell a drug for an intended use that is unapproved. *Id.* at 228. *Amarin* explained that, while "truthful and non-misleading statements" could in theory "serve as evidence of intent," the government would also need to identify some

"promotional action[] *other than truthful speech*." *Id.* (emphasis added). If the *only* "evidence" of off-label promotion is truthful and non-misleading speech, the prosecution is unlawful. *Id.*

Amarin also explained why this understanding of the First Amendment would not have the effect of forbidding misbranding prosecutions altogether. For one thing, "the First Amendment does not protect *false or misleading* commercial speech." *Id.* For another, a "manufacturer that engages in *non-communicative activities* to promote off-label use cannot use the First Amendment as a shield." *Id.* "*Caronia* holds protected, and outside the reach of the FDCA's misbranding provisions, off-label promotion only where it wholly consists of truthful and non-misleading speech." *Id.*

3. *Caronia* and *Amarin* correctly applied Supreme Court precedent, and this Court should adopt their approach. Indeed, as noted, since those cases were decided, the Supreme Court has only strengthened the protections applicable to truthful, non-misleading commercial speech. *Supra* pp. 6-7. The Court's recent cases make clear that prosecutions based on truthful, non-misleading speech about the uses of drugs and medical devices are subject to strict scrutiny. Under FDA's interpretation of its regulations, a manufacturer whose product has multiple lawful, medically accepted uses may speak only about certain uses—those that FDA has endorsed. "That is about as content-based as it gets." *AAPC*, 140 S. Ct. at 2346

(plurality op.). The restrictions "appl[y] to particular speech because of the topic discussed or the idea or message expressed." *Reed*, 576 U.S. at 163. The government here did not even attempt to defend these restrictions under the applicable strict-scrutiny framework and could not do so if it tried.

II. The Convictions Here Violated the First Amendment

Under Supreme Court precedent barring the use of protected speech to transform lawful conduct into unlawful conduct, and under *Caronia* and *Amarin*, the government needed to identify some criminal act "other than truthful speech" to sustain the convictions for misbranding and adulteration. *Amarin*, 119 F. Supp. 3d at 228; *see Caronia*, 703 F.3d at 161. Accordingly, this Court should not affirm unless it can point to evidence of a non-communicative act that constituted sufficient evidence that defendants intended to market the device for an unapproved use. If there would be no crime but for truthful, non-misleading speech about the off-label use, then there can be no valid conviction. Accepting the jury's findings here as true, the convictions cannot be reconciled with the First Amendment and should be vacated.

1. The jury in this case rejected the government's contention that defendants engaged in false or misleading speech. In addition to the misdemeanor charges on which defendants were convicted, the government charged felony misbranding and adulteration, which required proof of "specific intent to mislead

or defraud." Add.10 (quotation marks omitted). The jury acquitted on all felony charges, meaning, as the district court explained, that the jury found no "intent to mislead." *Id.*

Nor did the misbranding or adulteration convictions rest on any non-speech act. In affirming the misdemeanor convictions, the district court identified no criminal act beyond the defendant's promotion of the device for an unapproved use—*i.e.*, nothing "other than truthful speech" about its potential unapproved use. *Amarin*, 119 F. Supp. 3d at 228. In fact, the court's First Amendment analysis explicitly assumes that "the evidence of intended use consisted of *only* truthful, non-misleading speech and internal communications." Add.33 (emphasis added). The cited evidence of intent consisted of internal company communications, as well as statements at forums, marketing meetings, and internal and external training sessions. Add.18-31. The government, too, treated speech as the difference-maker, arguing that defendants "caused the distribution of the [device] for drug delivery *by making external marketing claims*" that the device was designed for the unapproved use. Opp. to Mot. Judgment of Acquittal, Dkt. 497, at 28 (Sept. 30, 2016) (emphasis added). The dispositive factor in this case was thus truthful, non-misleading communications of the exact sort that courts have held protected. *See Caronia*, 703 F.3d at 156 (promotional statements endorsing off-label use at programs for and meetings with physicians); *see also Ocheesee*

Creamery, 851 F.3d at 1237-38. Defendants' convictions thus violated the First Amendment.

2. Not only did the government offer no evidence beyond protected speech that could have established a wrongful intent, but the jury instructions also erroneously permitted the jury to convict on the basis of protected speech. To be sure, the instructions did not, as in *Caronia*, "flatly state[] to the jury that pharmaceutical representatives are prohibited from engaging in off-label promotion." 703 F.3d at 161. But the court here instructed the jury that, although "[t]ruthful, non-misleading speech cannot be a criminal act in and of itself," "it can be evidence and therefore used by you to determine whether the government has proved *each element of each offense beyond a reasonable doubt*, including the element of intent." Add.74 (emphasis added). Nor did the court instruct the jury that it needed to find any of defendants' speech false or misleading in order to convict them. In other words, the jury was told that protected speech was probative not only of intent, but also of whether the defendant had engaged in an act of misbranding or adulteration. And, critically, the jury was not told that it was required to find that defendants engaged in some *non-speech act* before concluding that they failed to obtain necessary clearance or approval for a new intended use. Rather, and contrary to precedent, if the jury had found that defendants' speech was the sole evidence of an unapproved intended use, that would suffice under the

court's instructions to support a conviction. No less than in *Caronia*, the government and the court's instructions "criminaliz[ed] the truthful off-label promotion of FDA-approved prescription drugs." *Caronia*, 703 F.3d at 168.

3. The district court sought to distinguish *Caronia* and *Amarin* on the theory that defendants engaged in a non-speech "actus reus" for each offense, namely, "the distribution of the device" without submitting "a premarket notification for the intended use of drug delivery." Add.34-36. In the court's view, defendants' speech was not "itself the crime," but instead was "evidence of [their] intent that the device be used for a purpose that the FDA had not approved." *Id.*

At the outset, *Caronia* did not, as the district court suggested, authorize this use of "[o]ff-label promotional statements" as "evidence of an intended use of a drug that the FDA has not approved." Add.34-35 (quoting *Caronia*, 703 F.3d at 155). To the contrary, *Caronia* "assume[d], *without deciding*, that such use of evidence of speech is permissible." 703 F.3d at 162 at n.9 (emphasis added); *accord United States ex rel. Polansky v. Pfizer, Inc.*, 822 F.3d 613, 615 n.2 (2d Cir. 2016) (*Caronia* "left open" government's use of speech as evidence of intent where the crime involves an independent actus reus). But it made clear that, even if use of speech as evidence is sometimes permissible, speech cannot be the *sole* evidence transforming lawful conduct into unlawful conduct. *Caronia*, 703 F.3d at

161 (jury led to "believe that Caronia's promotional speech was, by itself, determinative of his guilt").

That feature of defendants' convictions—that speech was the sole evidence used to transform lawful conduct into unlawful conduct—distinguishes this case from *Wisconsin v. Mitchell*, 508 U.S. 476 (1993), on which the district court relied. As the district court noted (Add.33), *Wisconsin* held that the "First Amendment … does not prohibit the evidentiary use of speech to establish the elements of a crime or to prove motive or intent." *Id.* at 489. But in *Wisconsin*, the defendant was convicted of assaulting a victim whom he deliberately chose based on race. *Id.* at 479. The state had criminalized "bias-inspired conduct" regardless of what the defendant did or did not say, and his statements were merely evidence of that independent impermissible act. *Id.* at 487-88.

The district court's conclusion that the "distribution" of the device was an independent criminal act here cannot be squared with the regulatory scheme or the actual holdings of *Caronia* or *Amarin*, and indeed would render the relevant constitutional principles meaningless. The basic problem with the district court's theory is that distributing the device is not itself a crime and using the device off-label is not itself a crime. Put differently, defendants could not have been prosecuted for distributing the device had they not engaged in promotional speech. And if speech is the sole evidence that transforms permissible conduct into

impermissible conduct, it is the speech—not some non-speech act—that has been made criminal. The government cannot "characteriz[e] its restriction as a regulation of speech relating to unlawful conduct because [defendants'] conduct is not unlawful, only [their] speech is." *Ocheesee Creamery*, 851 F.3d at 1238.

Moreover, in a misbranding or adulteration case, the manufacturer will always have "distribut[ed] the device." Add.36. The company in *Amarin*, for example, sought to distribute its product in interstate commerce and "to make truthful statements to doctors relating to [the product's] off-label use." 119 F. Supp. 3d at 198. And the defendant in *Caronia* "was found guilty of conspiracy to introduce a misbranded drug into interstate commerce." 703 F.3d at 152.

Indeed, the jury in *Caronia* was specifically instructed that a necessary element of the crime was "that the defendant conspired to introduce or conspired to cause to be introduced a drug into interstate commerce"—unquestionably a non-expressive act. *Id.* at 172 (Livingston, J., dissenting). Because the offense required proof of this action, both the government and the dissenting judge in *Caronia*—like the government here—asserted that the defendant's promotional statements were not being criminalized, but rather were permissibly being used as evidence that the non-speech act was performed "with the intent that [the drug] be used for purposes not supported by their labeling." *Id.* at 177.

The *Caronia* majority emphatically disagreed. It recognized that when the sole evidence of an unapproved intended use derives from the manufacturer's truthful, non-misleading promotional statements, a conviction is functionally equivalent to directly "criminalizing … truthful off-label promotion." *See id.* at 168 (majority opinion); *id.* at 174 (Livingston, J., dissenting) ("The majority's conclusion, clearly stated, is that while speech might serve as evidence of other types of mislabeling, such as false or deficient labeling, a mislabeling charge simply may not rest on off-label promotion.").

Amarin, too, unequivocally rejected the district court's theory here that the mere act of distribution could be a sufficient actus reus. In "illustrat[ing]" a conviction that might be lawful, the court cited "a misbranding prosecution of a manufacturer based on promotional actions *other than truthful speech*." 119 F. Supp. 3d at 228 (emphasis added). It was these sorts of non-expressive "*promotional actions*"—*not* mere distribution—that could potentially be "a proper *actus reus*." *Id.*; *cf.* Add.35. After all, the manufacturer's speech in both *Caronia* and *Amarin* could have been characterized merely as evidence that the party intended to distribute the drug for an unapproved use. But both courts properly recognized that this interpretation would infringe upon core First Amendment values.

In fact, the decision below made precisely the same error that the Supreme Court corrected in *Expressions Hair Design*. Just like FDA did not forbid the sale of the device here, or its prescription for unapproved uses, the law in *Expressions Hair Design* did not regulate merchants' prices or forbid surcharges. The court of appeals viewed the law as simply "regulating the relationship between two prices"—cash and credit—and thus regulating "conduct, not speech." 137 S. Ct. at 1150. But because the law was targeted at how the prices were conveyed, the Supreme Court held, it regulated speech, not conduct. *Id.* at 1151. The prohibited act was the characterization of a higher credit-card price *as a surcharge*. So too in *Cohen*, where the defendant's conviction under a facially neutral statute regulating breaches of the peace "rest[ed] solely upon speech." 403 U.S. at 18-19 (quotation marks omitted). Because Cohen had performed no independently illegal act, the conviction was subject to heightened scrutiny and could not survive that scrutiny. *See id.*

A misbranding or adulteration prosecution that turns on truthful, non-misleading speech—whether that speech is described as evidence of wrongful intent or as the actus reus itself—operates in the same improper way. The lawful action of distributing an FDA-cleared product *becomes illegal* solely because the manufacturer makes truthful statements about unapproved uses. That is not regulating the conduct of distribution; it is regulating "how sellers may

communicate" about the product being distributed. *Expressions Hair Design*, 137 S. Ct. at 1151. And the fact that it might be possible to bring a prosecution that does not depend on speech—just as the statute in *Cohen* could be violated in ways that did not depend on speech—does not save a prosecution that *does* depend on speech. "[T]he conduct triggering coverage under the [misbranding and adulteration laws] consists of communicating a message." *Humanitarian Law Project*, 561 U.S. at 28.

Thus, to affirm the convictions, this Court would need to identify some non-speech acts that were sufficient to establish intent beyond a reasonable doubt. Affirming under any other circumstances would violate the First Amendment and create a circuit split.

4. Compounding the First Amendment problem in this case is the fact that FDA's "intended use" regulations are hopelessly vague. The district court itself acknowledged that the government obtained these convictions only by "patching together the misbranding and adulteration regulations, thereby criminalizing conduct that it is not entirely clear Congress intended to criminalize." Add.6. That is because, as explained, the regulations do not directly prohibit making statements about unapproved uses; rather, criminal liability turns exclusively on whether the manufacturer "intended" a use that FDA did not approve. Due process thus, at a minimum, requires FDA's definition of "intended

use" to be sufficiently clear and unambiguous so as to give manufacturers "fair notice of what is prohibited." *FCC v. Fox Television Stations, Inc.*, 567 U.S. 239, 253 (2012) (quotation marks omitted). "When speech is involved, rigorous adherence to [due process] requirements is necessary to ensure that ambiguity does not chill protected speech." *Id.*

FDA's definition of an "intended use" does not provide fair notice. The governing regulations define "intended use" as "the objective intent of the persons legally responsible for the labeling of devices," which "may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives" or evidence "that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised." 21 C.F.R. § 801.4.

Although some courts hold that objective intent turns only on external marketing representations—capacious as that category is—the court here found that "the plain language of the regulation" authorized the use of "*any* 'oral or written statements' and 'circumstances,' whether directed internally or externally." Add.43. Under the district court's interpretation, manufacturers are left to guess at how many communications (and what type) will suffice to make a potential use of their product "intended," let alone to predict how FDA will view conflicting communications. This regime not only "fails to provide a person of ordinary

intelligence fair notice of what is prohibited," it is also "so standardless that it authorizes or encourages seriously discriminatory enforcement." *Fox*, 567 U.S. at 253. Does an internal email discussing the fact that doctors prescribe a particular medicine for an unapproved use subject a company to prosecution? It is impossible to know—and enforcement is subject to the government's whim. Worse, the regulation states that the types of evidence that it lists are only "example[s]." 21 C.F.R. § 801.4.

Regulations fail to provide fair notice if they "delegate[] basic policy matters to [government officials] for resolution on an ad hoc and subjective basis," *Grayned v. City of Rockford*, 408 U.S. 104, 108-09 (1972), or impose "a standard so indefinite that [lawmakers are] free to react to nothing more than their own preferences," *Smith v. Goguen*, 415 U.S. 566, 578 (1974). The criminalization of any "oral or written statement[]" that the government deems to provide evidence of an intended use fails the constitutional test. The inevitable result: manufacturers are chilled from communicating medically beneficial information about unapproved uses. While the First Amendment forbids restriction of this speech regardless, the vagueness of this scheme underscores the constitutional problems with using it to assign criminal liability.

III. Reversal Would Leave FDA With Significant Authority To Protect Public Health and Safety

Reversing these convictions—and barring the government from prosecuting manufacturers on the basis of their truthful, non-misleading speech about unapproved uses—would not disturb FDA's legitimate powers to protect public health and safety. As *Caronia* and *Amarin* observed, strict application of the First Amendment here leaves FDA with robust authority to ensure the safety and effectiveness of products that FDA regulates. What the First Amendment protects is truthful, non-misleading speech about potential off-label uses of approved products. By contrast, the First Amendment "does not protect *false or misleading*" speech about those products. *Amarin*, 119 F. Supp. 3d at 228.

The government's legitimate interest in preventing false or misleading claims about drugs and medical devices allows for serious, substantive limitations on manufacturers' promotional statements, so long as those limitations are stated clearly and do not impermissibly punish truthful, non-misleading speech. For example, manufacturers' communications could be deemed misleading if they fail to disclose the lack of FDA approval when the manufacturer speaks about studies of its products for uses not approved. Manufacturers might be required to disclose known safety risks about unapproved uses. And manufacturers might be required to accurately represent the data about unapproved uses and to provide appropriate context, including limitations of the data and the analyses conducted. Such context

may include biases in any analysis, problems with a study's methodology, contrary evidence, or the absence of statistical significance, among other things. These are just some examples of the ways in which the government's interests could be protected consistent with the First Amendment.

And if manufacturers make false or misleading promotional claims to third parties, the First Amendment as applied in *Caronia* and *Amarin* would not prohibit using those unsubstantiated claims as evidence that the manufacturer was engaged in misbranding or adulteration, so long as FDA regulations provided clear notice that such claims could support liability. PhRMA has accordingly encouraged FDA to adopt a regulatory framework that provides clear guidelines for manufacturers. *E.g.*, PhRMA, Comment, *Regulations Regarding "Intended Uses,"* FDA-2015-N-2002, at 3, 12 (Oct. 23, 2020), https://www.regulations.gov/comment/FDA-2015-N-2002-2050. Enforcing foundational First Amendment principles to preclude the criminal prohibition of truthful and non-misleading speech, like the speech underlying defendants' convictions, would not prevent FDA from safeguarding against those sorts of unsubstantiated promotional claims.

CONCLUSION

The Court should reverse the judgment of the district court.

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Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32 because the brief contains 6,486 words, excluding the parts of the brief exempted by Rule 32(f). This brief complies with the typeface and type style requirements of Rule 32(a)(5) and Rule 32(a)(6), respectively, because this brief has been prepared in a proportionately spaced typeface using Microsoft Word for Office 365 in Times New Roman 14-point font.

Dated: July 28, 2021

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CERTIFICATE OF SERVICE

I hereby certify that on July 28, 2021, the foregoing brief was electronically filed with the Court via the appellate CM/ECF system, and that copies were served on all counsel of record by operation of the CM/ECF system on the same date.

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