No. 23-1016

In the Supreme Court of the United States

WILLIAM FACTEAU AND PATRICK FABIAN, PETITIONERS

v.

UNITED STATES OF AMERICA

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FIRST CIRCUIT

BRIEF FOR THE UNITED STATES IN OPPOSITION

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QUESTIONS PRESENTED

1. Whether the government's use at trial of petitioners' statements, in a prosecution for distributing an adulterated or misbranded medical device, 21 U.S.C. 331(a), violated the First Amendment.

2. Whether the regulation illustrating how the "intended use" of a medical device may be determined violates the Due Process Clause of the Fifth Amendment.

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OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1-74) is reported at 89 F.4th 1. The order of the district court (Pet. App. 93-169) is not published in the Federal Supplement but is available at 2020 WL 5517573.

JURISDICTION

The judgment of the court of appeals was entered on December 14, 2023. The petition for a writ of certiorari was filed on March 13, 2024. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

STATEMENT

Following a jury trial in the United States District Court for the District of Massachusetts, petitioners were each convicted on five counts of distributing an adulterated device and five counts of distributing a misbranded device based on a lack of premarket notifica-

tion, all in violation of 21 U.S.C. 331(a). Pet. App. 75-76, 84-85. Each was sentenced to time served with no supervision to follow and a fine. *Id.* at 78, 87. The court of appeals affirmed. *Id.* at 1-74.

1. The Federal Food, Drug, and Cosmetic Act (FDCA), ch. 675, 52 Stat. 1040 (21 U.S.C. 301 *et seq.*), as amended by the Medical Device Amendments of 1976, Pub. L. No. 94-295, 90 Stat. 539, establishes the framework for the regulation of medical devices. See *Medtronic, Inc.* v. *Lohr*, 518 U.S. 470, 475-477 (1996). Under the statute, medical devices are categorized into three classes based on the level of risk they pose of illness or injury. *Id.* at 476-477; see 21 U.S.C. 360c(a)(1)(A)-(C).

Class III devices present the highest risk "and therefore incur the * * * strictest regulation" administered by the Food and Drug Administration (FDA). *Buckman Co.* v. *Plaintiffs' Legal Committee*, 531 U.S. 341, 344 (2001). Before being distributed, a Class III device must go through a "rigorous" premarket approval process, in which an applicant (generally the manufacturer) "must provide the FDA with a 'reasonable assurance' that the device is both safe and effective" for its intended use. *Lohr*, 518 U.S. at 477 (citation omitted); see 21 U.S.C. 360e(d)(2); *Buckman*, 531 U.S. at 344-345 (describing the premarket approval process). By default, any device not introduced into the market before May 28, 1976, is deemed to be a Class III device that must therefore undergo the rigorous premarket approval process. 21 U.S.C. 360c(f)(1).

Congress also created certain exceptions, however, including that "[a] new device need not undergo premarket approval if the FDA finds it is 'substantially equivalent' to another device exempt from premarket approval." *Riegel* v. *Medtronic, Inc.*, 552 U.S. 312, 317

(2008) (quoting 21 U.S.C. 360c(f)(1)(A)(ii)); see, *e.g.*, 21 U.S.C. 360(*l*) and (m), 360j(g) (describing other exceptions). "The agency's review of devices for substantial equivalence is known as the § 510(k) process, named after the statutory provision describing the review." *Riegel*, 552 U.S. at 317; see 21 U.S.C. 360(k). The Section 510(k) process is substantially less onerous, and far speedier, than premarket approval. See *Lohr*, 518 U.S. at 478-479.

To be eligible for the Section 510(k) process, a device must have the same intended use as the predicate device to which substantial equivalence is shown. See 21 U.S.C. 360c(i)(1)(A); 21 C.F.R. 807.100(b)(1). A premarket notification for Section 510(k) clearance must include a "510(k) summary" that, among other things, identifies the predicate device, describes the new device, and specifies the intended use of the new device. 21 C.F.R. 807.87(h), 807.92(a)(3)-(5). The submitter of such a notification also must include "[p]roposed labels, labeling, and advertisements sufficient to describe the [new device], its intended use, and the directions for its use." 21 C.F.R. 807.87(e).

If a device that has previously received Section 510(k) clearance experiences a "major change or modification in the intended use of the device," the submitter must submit a further premarket notification that addresses the new intended use "at least 90 days before" the device is proposed to begin moving in interstate commerce with the new intended use. 21 C.F.R. 807.81(a) and (3). That notification must contain "appropriate supporting data to show that the manufacturer has considered what consequences and effects the change or modification or new use might have on the safety and effectiveness of the device." 21 C.F.R.

807.87(g). Without Section 510(k) clearance for the new intended use, the device must obtain standard premarket approval for that new intended use before moving in interstate commerce. Cf. 21 U.S.C. 360c(f) and (i); 21 C.F.R. 807.100; *Buckman*, 531 U.S. at 344-345.

The "intended use" of a medical device is based on "the objective intent of the persons legally responsible for the labeling" of the device, 21 C.F.R. 801.4, a standard that dates back to the regulation's initial promulgation in 1952, see 17 Fed. Reg. 6818, 6820 (July 25, 1952) ("the objective intent of the persons legally responsible for the labeling of drugs and devices"); see also 41 Fed. Reg. 6896, 6896 (Feb. 13, 1976) ("the objective intent of the persons legally responsible for the labeling of devices"). At the time of petitioners' conduct and trial, the applicable regulation provided that "intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article." 21 C.F.R. 801.4 (2016). "This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives." *Ibid.*

The intended-use regulation also provided that a manufacturer's objective intent "may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised." 21 C.F.R. 801.4 (2016). The regulation explained that "if a manufacturer knows, or has knowledge of facts that would give him notice that a device introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a device which accords with such other uses to

which the article is to be put." *Ibid.* The regulation now clarifies "that a firm would not be regarded as intending an unapproved new use for a device * * * based solely on that firm's knowledge that such device was being prescribed or used by health care providers for such use." 21 C.F.R. 801.4; 86 Fed. Reg. 41,383, 41,401-41,402 (Aug. 2, 2021) (final rule).

2. Petitioner Facteau is the former CEO, and petitioner Fabian is the former vice president of sales, of Acclarent, Inc., a medical device manufacturer. Pet. App. 8-9. During Facteau's tenure, he and other Acclarent officers approved a project to develop a device that could treat sinusitis (inflammation of the mucus membranes of the paranasal sinuses) in the ethmoid sinuses. *Id.* at 9 & n.5.

The resulting product, an ethmoid sinus "spacer" called Stratus, consisted of a small, perforated balloon attached to a catheter. Pet. App. 9. Once inserted into the ethmoid sinus cavity, the balloon could be inflated and filled with Kenalog-40, a topical steroid, which would over a two-week period diffuse out of the balloon's pores to bathe the ethmoid cavity. *Id.* at 10. The balloon's pores were specifically designed and calibrated for use with Kenalog. *Ibid.*

Facteau authorized a two-step regulatory strategy for Stratus. Pet. App. 10. Acclarent would first seek Section 510(k) premarket clearance for an intended use as a spacer to deliver saline solution to moisten the sinuses after sinus surgery, likening it to a predicate device (the Rains Frontal Sinus Stent) already cleared for that use. *Ibid.* Once that clearance was secured, Acclarent would then seek to modify the labeling to indicate an intended use to deliver Kenalog for diagnostic and therapeutic procedures. *Ibid.*

Acclarent pursued that strategy even though it had specifically designed Stratus to deliver Kenalog, not saline, and knew that Stratus could not effectively deliver saline. Pet. App. 10-11. For one thing, "the pores in the balloon were too large to allow saline—a much less viscous fluid than Kenalog—to gradually seep out over a two-week period"; for another, the "amount of saline that could fit in the Stratus balloon was also too small to be of much therapeutic value." *Id.* at 11; see *id.* at 10-11.

The FDA granted Section 510(k) clearance to Stratus for use as a post-surgical spacer to deliver saline. Pet. App. 11. About seven months later, Acclarent sent a letter to the FDA stating that it "would like to modify the indications for use" by changing the labeling to add that Stratus "is also indicated for use to irrigate the sinus space for diagnostic and therapeutic procedures." C.A. App. 3459 (emphasis omitted); see Pet. App. 11. Specifically, Acclarent "sought to modify the instructions for use to state that the user could inject either saline or some 'other therapeutic agent' into the catheter to inflate the balloon." Pet. App. 11. Acclarent claimed that its proposed change "d[id] not exceed the limitations of the" cleared use and that "a premarket notification via 510(k) is not required." C.A. App. 3459.

The FDA disagreed, explaining in its response that based on Acclarent's descriptions, "it appears that you have significantly changed or modified" the "intended use of the device." C.A. App. 4698, see Pet. App. 12. The FDA further explained that at a minimum, Acclarent "would 'need to submit a new 510(k)' and receive FDA clearance 'prior to marketing Stratus' with the proposed changes in intended use." Pet. App. 12 (brackets omitted); see C.A. App. 4698. And an FDA

medical officer who had been reviewing Stratus-related matters since 2006 believed that Stratus's proposed intended use as "a drug delivery indication would require a premarket approval application, rather than a simple 510(k) notification." Pet. App. 107-108.

Acclarent recognized that an application for premarket approval of Stratus for use with Kenalog or a Section 510(k) notification for that new intended use "would need to be supported by appropriate clinical studies." Pet. App. 12. But each of the clinical studies that Acclarent conducted had to be halted because of significant risk to its subjects or reports of adverse events. *Id.* at 12-13. Acclarent ultimately never "completed an approved study to support Stratus's use with Kenalog." *Id.* at 13. Nor did it ever "file[] a premarket [Section 510(k)] notification for that intended use." *Ibid.*

But despite obtaining neither premarket approval nor Section 510(k) clearance for an intended use with Kenalog, Acclarent began distributing Stratus for use with Kenalog in July 2008. Pet. App. 13. Among other things:

- At Facteau's direction, a panel session at the July 2008 meeting of the Sinus Forum (an annual conference) featured live demonstrations of Stratus being used with Kenalog by two surgeons. *Id.* at 13-14. The panel explained how Stratus was designed for Kenalog, and one of the surgeons demonstrated that "Stratus was not suited for its cleared use" with saline. *Id.* at 13.
- Acclarent developed a slide presentation characterizing Stratus as "a way to obtain sustained drug delivery" to the sinuses. *Id.* at 14.

- Both petitioners joined a conference call with sales and training personnel discussing how to present Stratus to surgeons as a Kenalog delivery device. *Ibid.*
- Acclarent's booth at a major conference of ear, nose, and throat (ENT) surgeons provided information on using Stratus with Kenalog, but did not discuss or demonstrate using Stratus with saline. *Id.* at 14-15.
- Internal trainings for sales representatives, which petitioners often led or spoke at, repeatedly taught trainees "that Stratus was designed to be used * * * to deliver Kenalog," while trainees "were not taught about any clinical benefit that Stratus could provide when used as a spacer with saline." *Id.* at 15.
- Acclarent provided sales representatives with a document, reviewed and approved by Fabian, explaining that "the only agent that works optimally with Stratus is Kenalog." *Id.* at 16 (brackets omitted).
- Sales representatives "were never given marketing materials for Stratus that described benefits from using the device as a spacer with saline," but were given a video and "'sell sheets'" depicting the Stratus balloon filled with Kenalog. *Id.* at 17.
- Sales representatives "uniformly stated that their pitches positioned Stratus as a device to deliver Kenalog, rather than as a spacer with saline," and "multiple ENT surgeons" "corroborated" that experience. *Ibid.*

- Acclarent provided trainings to surgeons that included a Fabian-approved slide presentation that "did not describe how to use Stratus for its cleared use" with saline, but did "tell surgeons how to use Stratus with Kenalog." *Id.* at 18.
- In the laboratory-based session of that training, "participating surgeons would usually learn to use Stratus by filling the balloon with Kenalog or coffee creamer, a substance that looks like the steroid." *Ibid.*

Those efforts "bore abundant fruit," as Stratus generated tens of millions of dollars in gross revenue for Acclarent. *Ibid.*

3. The FDCA criminally prohibits "[t]he introduction or delivery for introduction into interstate commerce of any * * * device * * * that is adulterated or misbranded." 21 U.S.C. 331(a); see *United States* v. *Sullivan*, 332 U.S. 689, 696 (1948). Violations are misdemeanors unless committed "with the intent to defraud or mislead." 21 U.S.C. 333(a); see *United States* v. *Dotterweich*, 320 U.S. 277, 281 (1943). A device is "adulterated" if, among other things, it is a Class III device that has not received the requisite premarket approval. See 21 U.S.C. 351(f)(1)(B). And a device is "misbranded" if, among other things, "a notice or other information respecting it was not provided as required by" Section 510(k). 21 U.S.C. 352(*o*).

A federal grand jury in the District of Massachusetts returned an 18-count indictment charging petitioners on five counts of commercially distributing an adulterated device, in violation of 21 U.S.C. 331(a); five counts of commercially distributing a misbranded device, also in violation of 21 U.S.C. 331(a); three counts of securities fraud, in violation of 15 U.S.C. 78j(b) and 78ff(a), 17

C.F.R. 240.10b-5, and 18 U.S.C. 2; four counts of wire fraud and attempted wire fraud, in violation of 18 U.S.C. 1343, 1349, and 2; and one count of conspiring to commit the offenses listed above, in violation of 18 U.S.C. 371. Indictment 21-31. The five adulteration and five misbranding counts were premised on ten separate shipments of Stratus between October 2009 and May 2011. Pet. App. 19. Before trial, the government dismissed the securities-fraud counts and one of the wire fraud counts. *Id.* at 76, 85.

A jury found petitioners guilty on the five adulteration and five misbranding counts, and not guilty on the conspiracy and remaining wire fraud counts. Pet. App. 76, 85. The jury found them guilty of the misdemeanor versions of the adulteration and misbranding offenses, declining to find that they committed those offenses with intent to defraud or mislead. See *id.* at 20. The district court rejected petitioners' motion for judgments of acquittal and sentenced petitioners to time served with no supervision to follow. *Id.* at 78, 87. Facteau was fined $1,000,000 and Fabian was fined $500,000. *Id.* at 80, 89.

4. The court of appeals affirmed. Pet. App. 1-74.

The court of appeals rejected petitioners' First Amendment challenge to the district court's jury instructions, which had permitted the jury to consider petitioners' promotional speech as evidence of Stratus's intended use. Pet. App. 22-38. The court of appeals explained that "as a general matter, the First Amendment does not apply to the 'evidentiary use of speech to establish the elements of a crime or to prove motive or intent.'" *Id.* at 24 (quoting *Wisconsin* v. *Mitchell*, 508 U.S. 476, 489 (1993)). And the court observed that its rejection of petitioners' challenge was "in alignment

with our sister circuits," as all of the "courts to consider the issue have uniformly concluded that using speech merely as evidence of a misbranding offense under the FDCA does not raise First Amendment concerns." *Id.* at 29.

The court of appeals also rejected petitioners' argument that the term "intended use" is unconstitutionally vague and did not give petitioners fair notice that their conduct was proscribed, in violation of due process. Pet. App. 45-59. The court observed that the "FDCA and its implementing regulations make clear that manufacturers must submit a new premarket notification before they commercially distribute a device for an intended use that represents a 'major change or modification in the intended use of the device' from the cleared use," *id.* at 49 (quoting 21 C.F.R. 807.81(a)(3)(ii)), and that the intended-use regulation's reference to "'objective intent'" invokes "a familiar and well-established concept in the law." *Ibid.* (citing *United States* v. *Williams*, 553 U.S. 285, 306 (2008)). And the court found that petitioners had fair notice that their statements could be used as evidence to establish Stratus's intended use, given that the appellate courts had "consistently" held that "relevant evidence of intended use can come from many sources" and that "the interpretation of the determinants of 'intended use' under which [petitioners] w[ere] prosecuted was not a novel and more expansive interpretation." *Id.* at 57-58.

ARGUMENT

Petitioners contend (Pet. 13-23) that they were convicted in violation of the First Amendment, on the theory that the jury was invited to find them guilty based solely on truthful speech about Stratus. They further contend (Pet. 23-30) that their convictions violate the

Due Process Clause of the Fifth Amendment, on the theory that the "objective intent" standard in the intended-use regulation arbitrarily and irrationally criminalizes a manufacturer's mere knowledge that others might use a medical device for an indication not approved or cleared by the FDA (a so-called "off-label" use). Those contentions lack merit, and the decision below does not conflict with any decision of this Court or another court of appeals. Moreover, this case would be a poor vehicle in which to address the questions presented because the government presented overwhelming evidence of petitioners' guilt beyond just their allegedly truthful speech about Stratus and their knowledge that it was being used off-label. No further review is warranted.

1. a. The court of appeals correctly rejected petitioners' First Amendment challenge to their convictions. Pet. App. 22-38. Petitioners assert that the intended-use regulation "allow[s] the government to base an off-label promotion prosecution exclusively on protected speech," and suggest that their convictions rest on such a theory. Pet. 13-14. Those claims lack merit.

i. Petitioners were not convicted for expressing truthful information about Stratus; they were convicted for introducing into interstate commerce a medical device that was "adulterated or misbranded." 21 U.S.C. 331(a); see Indictment 30-31. The five adulteration convictions were based on Stratus's having been "a Class III device that lacked an FDA-approved pre-market approval" for use with Kenalog. Indictment 30. And the five misbranding counts were based on there having been "no pre-market notification * * * provided for the device as required by section 510(k)" for use with Kenalog. Indictment 31; see Pet. App. 20 n.9. The jury was

instructed accordingly. See C.A. App. 2477-2478 ("A medical device is adulterated if it is a Class III device that is required to have but does not have an FDA-approved premarket approval or 'PMA' application for [the] particular intended use."); *id.* at 2480 ("[A] medical device is also misbranded if the manufacturer introduces the device into interstate commerce for an intended use that is significantly different from the use covered by its 510(k) clearance and without submitting a new premarket notification to the FDA regarding the different intended use.").

Far from allowing a finding of guilt based on truthful, non-misleading speech, the jury instructions in fact "told the jurors that, because 'it is not illegal in and of itself for a device manufacturer to provide truthful, not misleading information about an off-label use,' they may *not* find a defendant guilty 'based solely on truthful, non-misleading statements promoting an FDA-cleared or approved device, even if the use being promoted is not a cleared or approved use." Pet. App. 22-23 (emphasis added; brackets omitted). The district court's instructions instead allowed jurors to "consider truthful, non-misleading speech promoting off-label use as 'evidence' in determining 'whether the government has proved each element' of the charged adulteration and misbranding offenses, 'including the element of intent.'" *Id.* at 23.

ii. Petitioners' convictions were thus based on their actions to distribute Stratus for use with Kenalog, not any protected speech about Stratus. As the court of appeals observed (Pet. App. 25-30), this Court held in *Wisconsin* v. *Mitchell*, 508 U.S. 476 (1993), 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. *Mitchell* rejected a First Amendment challenge to a statute that increased the maximum sentence for an aggravated battery from two years of imprisonment to seven years if the defendant was motivated by the victim's race or other protected trait. See *id.* at 480. The Court acknowledged that evidence of such a motive often might include the defendant's prior speech, but observed that "[e]vidence of a defendant's previous declarations or statements is commonly admitted in criminal trials subject to evidentiary rules dealing with relevance, reliability, and the like," without raising First Amendment concerns. *Id.* at 489.

As illustrated by the jury instructions, petitioners' statements were used to establish their own intent to market Stratus for use with Kenalog despite failing to secure either premarket approval or Section 510(k) clearance for marketing the device for that intended use. See pp. 7-9, *supra*. As the court of appeals explained, "what [petitioners] said about Stratus simply shed light on how they intended it to be used." Pet. App. 28.

Petitioners attempt to distinguish *Mitchell* on the theory that the intended-use regulation "do[es] not use speech as evidence of some *other* criminal act," but instead establishes an element of the offense, whereas "Mitchell's battery was already a crime regardless of his motivation," and that motivation constituted only a sentencing enhancement. Pet. 22; see Pet. 22-23. But nothing in *Mitchell* turns on that putative distinction; to the contrary, *Mitchell* stated 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," 508 U.S. at 489 (emphasis added). Nor do petitioners provide any sound basis for drawing such a dis-

tinction. Cf. *Apprendi* v. *New Jersey*, 530 U.S. 466, 494 (2000) (rejecting a similar general distinction in the Sixth Amendment context).

iii. Petitioners' reliance (Pet. 14-16, 21) on *Sorrell* v. *IMS Health Inc.*, 564 U.S. 552 (2011), likewise is misplaced. There, the Court found that a state statute restricting the sale, disclosure, and use of certain pharmacy records was subject to heightened scrutiny because "[o]n its face" it imposed "content- and speaker-based restrictions on the sale, disclosure, and use of prescriber-identifying information." *Id.* at 563-564. Here, in contrast, nobody is permitted to introduce Class III medical devices into interstate commerce for a particular intended use without first obtaining FDA approval or clearance for that intended use. Indeed, one might view the prohibition on marketing such a device for an intended use different from the one approved or cleared by FDA as a reasonable and germane condition on obtaining that approval or clearance in the first place. Cf. *Rust* v. *Sullivan*, 500 U.S. 173, 193 (1991); *Regan* v. *Taxation With Representation*, 461 U.S. 540, 547-550 (1983).

More important, unlike the statute in *Sorrell*, the FDCA and the intended-use regulation do not directly regulate speech; they regulate economic activity—here, the flow in interstate commerce of potentially dangerous Class III medical devices—in a way that, at most, imposes incidental burdens on speech. Cf. *Expressions Hair Design* v. *Schneiderman*, 581 U.S. 37, 47 (2017); *Sorrell*, 564 U.S. at 567; *Rumsfeld* v. *Forum for Academic and Institutional Rights, Inc.*, 547 U.S. 47, 62 (2006). As noted above, the jury here was expressly instructed that "[i]t is *not* illegal in and of itself for a device manufacturer to provide truthful, not misleading

information about an off-label use"; that the "FDCA does *not* prohibit or criminalize truthful, not misleading off-label promotion"; and that "you may *not* convict * * * based solely on truthful, non-misleading statements regarding off-label use." C.A. App. 2464-2465 (emphases added).

iv. At all events, even if the FDCA and implementing regulations could be viewed as regulating speech as such, the judgment below may be affirmed on the alternative ground that the statute and implementing regulations would satisfy the First Amendment standard for regulation of commercial speech set forth in *Central Hudson Gas & Electric Corp.* v. *Public Service Commission*, 447 U.S. 557 (1980). See *Upper Skagit Indian Tribe* v. *Lundgren*, 138 S. Ct. 1649, 1654 (2018) (lower court's judgment may be affirmed "on any ground supported by the law and the record"). Under that standard, a regulation of commercial speech comports with the First Amendment either if "the commercial speech concerns unlawful activity or is misleading," or if the "'asserted governmental interest is substantial'" and the regulation "'directly advances'" that interest and "'is not more extensive than necessary to serve that interest.'" *Thompson* v. *Western States Medical Center*, 535 U.S. 357, 367 (2002) (citation omitted). Assuming for argument's sake that petitioners' prosecutions amount to a regulation of their speech, that regulation satisfies *Central Hudson*.

First, it is unlawful to distribute a Class III medical device in interstate commerce without obtaining the required approval or clearance for each intended use. See 21 U.S.C. 331(a). Speech promoting such distribution efforts thus "concerns unlawful activity." *Thompson*, 535 U.S. at 367; see *Nicopure Labs, LLC* v. *FDA*, 944

F.3d 267, 284 (D.C. Cir. 2019). Second, even setting that aside, the government has a substantial interest in protecting the public from potentially dangerous Class III medical devices. The relevant regulations—not just the intended-use regulation, but also those implementing the premarket approval and Section 510(k) clearance processes—directly advance that interest by ensuring that FDA has approved or cleared each intended use for such devices. And by regulating only the entities involved in distributing those devices (such as manufacturers, distributors, importers, et al.)—who are "best positioned to conduct the research and gather information necessary for premarket review"—the regulations are not more extensive than necessary to serve the government's interests. FDA, *Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products* 25 (Jan. 2017), www.regulations.gov/document/FDA-2016-N-1149-0040; see *id.* at 20-34; see also *Nicopure*, 944 F.3d at 284-290.

b. Petitioners err in contending (Pet. 34-35) that the decision below conflicts with the Second Circuit's decision in *United States* v. *Caronia*, 703 F.3d 149 (2012). *Caronia* reversed a misbranding conviction under the First Amendment because it found as a factual matter that "[e]ven assuming the government can offer evidence of a defendant's off-label promotion to prove a drug's intended use and, thus, mislabeling for that intended use, that is not what happened in this case." *Id.* at 161 (footnote omitted). The court found, among other things, that the prosecution's "assertion now that it used Caronia's efforts to promote [the drug] for off-label use only as evidence of intent is simply not true."

Id. at 161. Instead, after examining the trial record, the court determined that "the government clearly prosecuted Caronia for his words—for his speech," given that the government "did not * * * limit its use" of the defendant's speech simply to show intent or the intended use of the drug, and the district court itself "flatly stated to the jury that pharmaceutical representatives are prohibited from engaging in off-label promotion." *Ibid.*

In contrast, the jury here was expressly instructed that "promoting a device off-label[] * * * is not itself a crime" and that it could *not* find petitioners guilty based solely on their truthful speech regarding the off-label use of Stratus with Kenalog. C.A. App. 2465; see *id.* at 2464-2465; see also Pet. App. 23 (explaining that the jury was instructed that it could not find guilt on an adulteration or misbranding count "based solely on truthful, non-misleading statements promoting an FDA-cleared or approved device, even if the use being promoted is not a cleared or approved use"). And as the court of appeals here explained (Pet. App. 27-29), nothing in *Caronia* casts doubt on the principle that "the government can offer evidence of a defendant's off-label promotion to prove a drug's intended use and, thus, mislabeling for that intended use." *Caronia*, 703 F.3d at 161 (citing, *inter alia*, *Mitchell*, *supra*).

The court of appeals thus correctly recognized (Pet. App. 29) that its decision is "in alignment with our sister circuits—including the Second." Indeed, other courts of appeals that have addressed the issue "have uniformly concluded that using speech merely as evidence of a misbranding offense under the FDCA does not raise First Amendment concerns." *Ibid.*; see *Whitaker* v. *Thompson*, 353 F.3d 947, 952-953 (D.C. Cir.), cert. de-

nied, 543 U.S. 925 (2004); *United States* v. *LeBeau*, 654 Fed. Appx. 826, 830-831 (7th Cir. 2016), cert. denied, 580 U.S. 1126 (2017). The Second Circuit itself has confirmed that "*Caronia* left open the government's ability to prove misbranding on a theory that promotional speech provides evidence that a drug is intended for a use that is not included on the drug's FDA-approved label." *United States ex rel. Polansky* v. *Pfizer, Inc.*, 822 F.3d 613, 615 n.2 (2016). Accordingly, petitioners provide no sound basis to conclude that the Second Circuit would reverse their convictions on the First Amendment grounds they raise in the petition for a writ of certiorari.

c. At all events, this case would be a poor vehicle in which to address the first question presented. Most important, the government relied on extensive evidence of petitioners' intent and the intended use of Stratus that cannot be classified simply as truthful statements about Stratus's off-label use with Kenalog. See pp. 7-9, *supra* (cataloging some of that evidence). For example, the government's evidence established that Stratus was specifically designed for use with Kenalog and ineffective for use with saline, and that petitioners tailored their rollout of Stratus to position it solely as a product for dispensing Kenalog, not saline. See *ibid.* As the court of appeals observed, "this was not a close case." Pet. App. 50. Accordingly, the introduction of such statements as evidence of petitioners' intent would at most be harmless error. Cf. *Arizona* v. *Fulminante*, 499 U.S. 279, 306-307 (1991) (explaining that nearly all constitutional trial errors are subject to harmless-error analysis).

Moreover, although in this Court petitioners principally focus (Pet. 14-23) on the intended-use regulation,

in the lower courts they framed their First Amendment challenge as one to the jury instructions, not the regulation, see Pet. App. 22 (observing that petitioners' "First Amendment attack on [their] conviction[s] takes the form of an instructional challenge"); cf. *id.* at 21 n.10. Accordingly, this Court would have to address a direct challenge to the constitutionality of the intended-use regulation in the first instance. But see *Cutter* v. *Wilkinson*, 544 U.S. 709, 718 n.7 (2005) ("[W]e are a court of review, not of first view.").

2. Petitioners' separate due-process claim likewise was correctly rejected by the court of appeals, see Pet. App. 45-59, and does not warrant this Court's review.

a. i. Petitioners' principal claim in this Court—that the intended-use regulation is "irrational" and "a recipe for arbitrary enforcement"—rests on the premise that the regulation "make[s] it a crime to distribute an FDA-approved product based on nothing more than knowledge that it is used off-label." Pet. 24, 26; see Pet. 23-30. That premise is mistaken.

The jury here was expressly instructed that "[m]ere knowledge that doctors are using a device for purposes other than its labeled use does not give rise to a new intended use" and that "[m]erely distributing a device with knowledge that it will be used for a use other than the use cleared or approved by the FDA is not fraudulent or illegal." C.A. App. 2464, 2466. That is how the FDA has long interpreted its regulations. See, *e.g.*, 76 Fed. Reg. 82,303, 82,304 (Dec. 30, 2011) (notice of draft guidance); FDA, *Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices* 6 n.8 (Dec. 2011), www.fda.gov/media/82660/download (draft guidance addressing how firms may respond to unsolicited requests for infor-

mation about off-label uses, and explaining that the relevant "policy was articulated in a letter to industry in 1982" and subsequently "restated on many occasions"). There is thus no sound basis to conclude that petitioners were found guilty based on their mere awareness of off-label use here.

Petitioners incorrectly assert that the district court contradicted its instruction not to find guilt on that theory when it told the jury (1) that a person's objective intent "may be shown by the circumstances that the device is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised," and (2) that "if a manufacturer has received 510(k) clearance to distribute a device for one intended use, it may not distribute the device for a significantly different intended use unless it obtains a new 510(k) clearance or a [premarket] approval for the device with that new intended use." Pet. 25 (citations omitted); see C.A. App. 2464, 2466. But both of those additional statements are correct statements of the law and are not inconsistent with the instruction that mere knowledge of off-label use is insufficient to establish guilt.

The first refers to a defendant's knowledge that a device is "*offered and* used" for a purpose that FDA did not approve or clear, C.A. App. 2466 (emphasis added), which plainly refers to the defendant's own actions, not simply the off-label use of the device by physicians. And the second says nothing about knowledge at all; to the contrary, the repeated "distribute * * * for" language refers to the defendant's own marketing of the device, not simply knowledge of how physicians are using the device. *Id.* at 2464. And at all events, the district court's express instruction that "[m]ere knowledge" of off-label

use is insufficient to establish guilt resolves any ambiguity that those two statements otherwise might have created on their own. *Id.* at 2466.

ii. Petitioners also claim that FDA's enforcement "regime" is "'expansive,'" "vague," "'standardless,'" "all-encompassing," and "limitless," Pet. 26-28 (citations omitted); that it lacks "an ascertainable, legally meaningful line" and fails to provide "'fair notice'" to regulated entities, Pet. 26, 28 (citation omitted); and that the "FDA has never clearly explained" what is and is not prohibited, Pet. 29. Those claims lack merit.

The FDCA and the FDA's longstanding regulations implementing the 1976 amendments make clear that a Class III medical device manufacturer must obtain premarket approval or Section 510(k) clearance to market the device in interstate commerce for a particular intended use, and that a new intended use or major change to the intended use requires a new premarket approval or a Section 510(k) notification and clearance for that new intended use. See 21 U.S.C. 331, 351, 352, 360(k), 360c, 360e; 21 C.F.R. 801.4 and Pts. 807, 814. Petitioners do not identify anything vague or arbitrary about those restrictions.

Instead, petitioners take exception to the intended-use regulation, but that provision simply makes clear that a device's intended use is determined by "the objective intent of the persons legally responsible for the labeling of" the device, 21 C.F.R. 801.4. In the case of Stratus, petitioners are those persons. Petitioners object to the regulation's supposedly "oxymoronic" descriptor of "'objective intent,'" Pet. 27 (citation omitted), but that term is "a familiar and well-established concept" in this context, Pet. App. 49, dating back to FDA's original 1952 regulations, see 17 Fed. Reg. at

6820. As applied here, it clarifies that the intended use of a device may be established using objective evidence, such as "labeling claims, advertising matter, or oral or written statements," among other "circumstances surrounding the distribution of the article." 21 C.F.R. 801.4. As the court of appeals explained (Pet. App. 50), the list of illustrative examples might "cast[] a wide net," but "fairly apprises the reader of the broad range of conduct that may reasonably reflect a device's intended use," which is all that due process requires. See *United States* v. *Williams*, 553 U.S. 285, 304-306 (2008).

b. Petitioners do not assert that the court of appeals' resolution of their due-process claim conflicts with any decision of this Court or another court of appeals. Nor do petitioners identify any appellate decision calling into question the intended-use regulation. Those alone are sufficient reasons to deny further review of the second question presented. See Sup. Ct. R. 10. In any event, this case would be an inappropriate vehicle in which to address that question because the record unequivocally shows that petitioners themselves did not lack fair notice of what the FDCA and its implementing regulations required. See *Holder* v. *Humanitarian Law Project*, 561 U.S. 1, 20 (2010) ("[A] plaintiff who engages in some conduct that is clearly proscribed cannot complain of the vagueness of the law as applied to the conduct of others.") (citation omitted).

Petitioners specifically crafted a two-step regulatory approach with knowledge of those requirements. See Pet. App. 10-11. But after step one, the FDA expressly warned petitioners that their proposed distribution of Stratus for use with Kenalog was *not* covered by the existing Section 510(k) clearance and that, at a minimum, another Section 510(k) premarket notification seeking

clearance for that new intended use—if not an application for premarket approval—would be required. See C.A. App. 4698; Pet. App. 107-108. Petitioners knew they would need clinical studies to support either course, but that the clinical trials had ended prematurely. Pet. App. 12-13. Nevertheless, petitioners simply ignored the FDA's express warning and plowed ahead with their efforts to distribute and market Stratus for use with Kenalog without seeking premarket approval or Section 510(k) clearance for that use. *Id.* at 13-19. In those circumstances, petitioners cannot claim to be surprised or to have lacked fair notice that their actions violated the FDCA's prohibition on adulteration and misbranding.

In addition, although in this Court petitioners focus almost exclusively on the premise that the intended-use regulation impermissibly permits a defendant to be convicted based solely on his knowledge that a device is being used for off-label purposes, see Pet. 24-29, their due-process challenge in the lower courts was premised on the claim that the district court interpreted the regulations to permit an overly broad set of evidence to establish a device's intended use, cf. Pet. App. 48-59. The court of appeals thus had no occasion to address the knowledge argument, which this Court would have to address in the first instance, in contravention of its normal practice, see *Cutter*, 544 U.S. at 718 n.7.

Furthermore, effective September 2021, the FDA promulgated a final rule amending the intended-use regulation "to better reflect the Agency's current practices in evaluating whether * * * a medical product that is approved, cleared, granted marketing authorization, or exempted from premarket notification is intended for a new use." 86 Fed. Reg. at 41,384. As particularly rel-

evant here, the regulation now expressly clarifies "that a firm would not be regarded as intending an unapproved new use for a device * * * based solely on that firm's knowledge that such device was being prescribed or used by health care providers for such use." 21 C.F.R. 801.4. That regulatory clarification, which echoes the jury instructions in this case, substantially diminishes the importance of addressing petitioners' challenge to an obsolete version of the intended-use regulation.

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted.

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