United States Court of Appeals
For the First Circuit

No. 21-1080

UNITED STATES OF AMERICA,

Appellee,

v.

WILLIAM FACTEAU,

Defendant, Appellant.

No. 21-1082

UNITED STATES OF AMERICA,

Appellee,

v.

PATRICK FABIAN,

Defendant, Appellant.

APPEALS FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

[Hon. Allison D. Burroughs, U.S. District Judge]

Before

Gelpí, Lipez, and Thompson,
Circuit Judges.

Reid H. Weingarten, with whom William Hassler, Shannen W. Coffin, Bruce C. Bishop, Steptoe & Johnson LLP, Michael Pineault,

and Anderson & Krieger LLP were on brief, for appellant William Facteau.

Frank A. Libby, Jr., with whom Brian J. Sullivan, and Libby Hoopes Brooks, P.C. were on brief, for appellant Patrick Fabian.

Randall E. Kromm, Assistant United States Attorney, with whom Nathaniel R. Mendell, Acting United States Attorney, was on brief, for appellee.

Joel Kurtzberg, Adam S. Mintz, John S. MacGregor, Jason Rozbruch, Cahill Gordon & Reindel LLP, Cory L. Andrews, John M. Masslon II, and Washington Legal Foundation on brief for Washington Legal Foundation, amicus curiae.

Douglas Hallward-Driemeier, Kelli B. Combs, Joan McPhee, Ropes & Gray LLP, Paul E. Kalb, Coleen Klasmeier, Erika L. Maley, and Sidley Austin LLP on brief for Amgen Inc., Biosplice Therapeutics, Inc., Boehringer Ingelheim Pharmaceuticals, Inc., Bristol Myers Squibb Company, Eli Lilly and Company, GlaxoSmithKline LLC, Novartis Pharmaceuticals Corporations, and Pfizer Inc., amici curiae.

Jeffrey S. Bucholtz, Michael R. Pauzé, John C. Richter, Alexander Kazam, and King & Spalding LLP on brief for Howard Root, amicus curiae.

Jeffrey L. Handwerker, Elisabeth S. Theodore, Samuel F. Callahan, Arnold & Porter Kaye Scholer LLP, James C. Stansel, Melissa B. Kimmel, and Kelly Goldberg on brief for Pharmaceutical Research and Manufacturers of America, amicus curiae.

Jeffrey L. Handwerker, Elisabeth S. Theodore, Samuel F. Callahan, Arnold & Porter Kaye Scholer LLP, Daryl Joseffer, Andrew R. Varcoe, and U.S. Chamber Litigation Center on brief for Chamber of Commerce of the United States of America, amicus curiae.

December 14, 2023

LIPEZ, Circuit Judge. After a thirty-day jury trial, appellants William Facteau and Patrick Fabian, former executives of the medical device manufacturer Acclarent, Inc., were found guilty of multiple misdemeanor violations of the Federal Food, Drug, and Cosmetic Act ("FDCA") for commercially distributing an adulterated and misbranded medical device. See 21 U.S.C. § 331(a). The charges related to a device developed and sold by Acclarent that the government alleged served an intended use different from the one for which it had been cleared by the U.S. Food and Drug Administration ("FDA").

On appeal, appellants assert that their prosecutions violated their First Amendment rights, relying on an emerging body of law protecting commercial speech that promotes off-label uses of medical products. Appellants also argue that their convictions violated due process under the Fifth Amendment. Fabian further contends that the jury was wrongly instructed about what evidence it could consider, that the evidence was insufficient to support his conviction, and that the $500,000 fine the court imposed on him is excessive under the Eighth Amendment.

We reject all of these claims and affirm.

I.

The FDCA strictly limits the ways in which manufacturers may market medical devices, including a prohibition on the distribution of "adulterated" or "misbranded" devices. A device

is adulterated or misbranded if its "intended use" -- as determined objectively by the seller's statements and conduct -- differs from the use(s) for which the FDA has cleared it.

Facteau, former CEO of Acclarent, and Fabian, the company's former vice present of sales, played prominent roles in the marketing of a new device for the treatment of chronic sinusitis, the Relieva Stratus Microflow Spacer ("Stratus"). Acclarent obtained preliminary approval to market Stratus for use as a "spacer" that would dispense a saline solution to the ethmoid sinuses and maintain an opening created by sinus surgery. Facteau and Fabian were convicted of unlawfully marketing Stratus to dispense a steroid, an "off-label" (i.e. unapproved) use, and fined $1 million and $500,000, respectively.

A. Legal Framework Governing Medical Devices

The FDCA has prohibited the distribution of adulterated or misbranded medical devices since its original enactment in 1938. With the Medical Device Amendments of 1976 ("MDA"), Pub. L. No. 94-295, 90 Stat. 539, "[i]n response to the mounting consumer and regulatory concern" over the lack of premarket review of medical devices, Congress broadened the statute's coverage to regulate the introduction of new medical devices to the market as well. Medtronic, Inc. v. Lohr, 518 U.S. 470, 476 (1996). This statutory scheme classifies "devices intended for human use" based on the level of risk to the public, with Class III devices presenting the

most risk and correspondingly incurring the strictest regulation. 21 U.S.C. § 360c(a)(1)(C); see Lohr, 518 U.S. at 476-77; Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 343-44 (2001). Devices not on the market before 1976 -- and thus all new devices -- are initially placed by default in Class III. 21 U.S.C. § 360c(f)(1).

1. Premarket Approval and § 510(k) Clearance

Class III devices must receive "premarket approval" ("PMA") from the FDA before they can legally be marketed. See § 360e(a)(2). The PMA process is "time-consuming," Buckman, 531 U.S. at 348, because it requires the device's manufacturer to demonstrate a "reasonable assurance" that the device is safe and effective, id. at 344. See also Lohr, 518 U.S. at 477.

A new device can avoid PMA review, however, if the FDA clears it through the "premarket notification" or "§ 510(k)" process,[1] which results in the device's reclassification from Class III to Class I or II. Lohr, 518 U.S. at 478-79. A new device can obtain § 510(k) clearance if the FDA determines that it is "substantially equivalent" to a predicate device -- that is, a pre-1976 device or a post-1976 device that previously was moved from Class III to Class I or II. See § 360c(f)(1)(A)(ii); 21

[1] The "§ 510(k)" label for the premarket notification process reflects the original MDA section number for the process. See Lohr, 518 U.S. at 478. That provision of the MDA is now codified at 21 U.S.C. § 360(k).

C.F.R. § 807.92(a)(3); Buckman, 531 U.S. at 345. A new device is "substantially equivalent" to a predicate device if it (1) has the "same intended use" and (2) either has the same technological characteristics or the same safety and effectiveness profile. 21 U.S.C. § 360c(i)(1)(A); 21 C.F.R. § 807.100(b).

At least ninety days before introducing a new device to the market, a manufacturer seeking § 510(k) clearance must submit a premarket notification to the FDA. 21 C.F.R. § 807.81(a). This premarket notification submission includes a "510(k) summary" identifying the predicate device and describing the device submitted for clearance, including its "intended use." 21 C.F.R. §§ 807.87(h), 807.92(a)(3)-(5).[2] The submission must also contain "[p]roposed labels, labeling, and advertisements sufficient to describe the [device submitted for clearance], its intended use, and the directions for its use." Id. § 807.87(e).

2. "Intended Use"

If the manufacturer of a device that is being marketed after receiving § 510(k) clearance makes a "major change or modification" in the device's intended use, the manufacturer must

[2] Instead of a 510(k) summary, the manufacturer may choose to submit a "510(k) statement" certifying that, if the FDA concludes that the device submitted for clearance is substantially equivalent to a predicate device, the manufacturer will provide safety and effectiveness information to support the FDA's finding within thirty days of a written request. See 21 C.F.R. §§ 807.87(h), 807.93.

submit another premarket notification at least ninety days before marketing the device for the new use. 21 C.F.R. § 807.81(a)(3)(ii). This new notification must include supporting data showing that the manufacturer has considered the "consequences and effects the . . . new use might have on the safety and effectiveness of the device." Id. § 807.87(g).

Whereas the FDA determines the intended use of a new device based solely on the proposed labeling submitted with its premarket notification, see 21 U.S.C. § 360c(i)(1)(E)(i), it determines the intended use of a device already cleared for commercial distribution by reference to the "objective intent of the persons legally responsible for the labeling" of the device ("labelers"), 21 C.F.R. § 801.4 (2020).[3] Labelers' "expressions" -- such as "labeling claims, advertising matter, or oral or written statements by [labelers] or their representatives" -- are one source of evidence for determining their "objective intent." Id. Labelers' "objective intent" may also be established by the "circumstances surrounding the distribution" of the device. Id.

[3] We refer to the version of the regulation governing the "intended use" of devices already on the market that was in effect at the time appellants took the actions underlying their convictions. The regulation was revised in August 2021. See Regulations Regarding "Intended Uses", 86 Fed. Reg. 41401-02 (Aug. 2, 2021) (codified at 21 C.F.R. § 801.4).

3. Adulteration, Misbranding, and Off-label Use

The FDCA prohibits the "introduction or delivery for introduction into interstate commerce of any . . . device . . . that is adulterated or misbranded." 21 U.S.C. § 331(a). Violating this prohibition "with the intent to defraud or mislead" is a felony; a violation absent such intent is a misdemeanor. Id. §§ 333(a)(1)-(2). Misdemeanor offenses of commercially distributing adulterated or misbranded devices are strict-liability crimes. United States v. Dotterweich, 320 U.S. 277, 284 (1943).

A device is "adulterated" under § 351(f)(1)(B) if, as a Class III device, it is "required to have in effect an approved application for premarket approval" but moves in interstate commerce without the required PMA. See also United States v. Universal Mgmt. Servs., Inc. Corp., 191 F.3d 750, 754 (6th Cir. 1999). When a device that received an initial § 510(k) clearance is marketed for an intended use that represents a "major change or modification" from the cleared use without clearance for that change, the device is also considered "adulterated." 21 C.F.R. § 807.81(a)(3)(ii). As relevant here, a device is "misbranded" if the manufacturer fails to submit a "notice" to the FDA "as required by . . . section 360(k)." 21 U.S.C. § 352(o). The "notice" referenced by the statute is the new premarket notification required when a device that previously received § 510(k) clearance

is about to have a "major change or modification in [its] intended use." 21 C.F.R. § 807.81(a)(3)(ii).

In sum, it is unlawful for a manufacturer to commercially distribute a device for an intended use that represents a "major change or modification" from the specific use for which the device received § 510(k) clearance. Such off-label marketing would amount to the commercial distribution of an "adulterated" and "misbranded" device. At the same time, however, the FDCA expressly protects the "authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease . . . ." 21 U.S.C. § 396.[4] Accordingly, medical professionals may lawfully prescribe and administer a device for an off-label use as long as that device has received § 510(k) clearance for any intended use. See Buckman, 531 U.S. at 350; Judge Rotenberg Educ. Ctr., Inc. v. U.S. Food & Drug Admin., 3 F.4th 390, 395 (D.C. Cir. 2021). The statutory and regulatory scheme governing medical devices thus limits the commercial distribution of devices to ensure that devices on the market are reasonably safe and effective, while preserving health care

[4] We note that this section of the FDCA does contemplate some limitations on the authority conferred on health care providers with respect to "legally marketed device[s]." Section 396 states that the FDA's mandate not to interfere with the practice of medicine does not limit the agency's authority "to establish and enforce restrictions on the sale or distribution, or in the labeling, of a device . . . ." 21 U.S.C. § 396.

professionals' discretion to prescribe and administer devices as they deem appropriate. See Buckman, 531 U.S. at 349-50.

B. Factual Background

Appellants' various claims on appeal require us to present the facts from two different perspectives. See United States v. Burgos-Montes, 786 F.3d 92, 99 (1st Cir. 2015). When recounting the evidence relevant to Fabian's sufficiency-of-the-evidence challenges, we take the facts in the light most favorable to the verdict. See United States v. Chan, 981 F.3d 39, 45 (1st Cir. 2020). For the other issues on appeal, we present the facts in a "balanced" way, taking an "objective[] view" of the evidence in the record. Burgos-Montes, 786 F.3d at 99 (first quoting United States v. Felton, 417 F.3d 97, 99 (1st Cir. 2005); then quoting United States v. Nelson-Rodríguez, 319 F.3d 12, 23 (1st Cir. 2003)).

1. Development and Design of Stratus

Acclarent was founded in 2004 as a medical device manufacturer focusing on devices for use in ear, nose, and throat ("ENT") care. Facteau served as Acclarent's CEO from November 2004 to December 2011, and Fabian was the company's vice president of sales from August 2007 to November 2011. Since its founding, Acclarent's core products have been devices for use in balloon

sinuplasty, a surgical technique to treat chronic sinusitis by dilating the sinus openings with a small balloon.[5]

However, sinusitis in the ethmoid sinuses is not treatable with balloon sinuplasty. As early as 2005, therefore, the members of Acclarent's Scientific Advisory Board ("SAB"), led by Facteau, discussed the possibility of developing a device that could provide relief for ethmoid sinusitis by delivering Kenalog-40 ("Kenalog") -- a topical steroid commonly used to reduce sinus inflammation -- directly to the ethmoid sinuses. These discussions culminated in the January 2006 approval by Facteau and other Acclarent officers of a project aimed at developing an "Ethmoid Sinus Stent" that, in the words of the project specification prepared as a roadmap for the design process, would be able "to deliver . . . Kenalog 40 for a duration of 14 days" "to the ethmoid [sinuses]."

This project led to the design of a device that was ultimately marketed as Stratus. The device featured a small balloon that was perforated with many tiny pores and was attached to a catheter. The device would be inserted, with the balloon

[5] Sinusitis is the inflammation of the mucus membranes of the paranasal sinuses, see Stedman's Medical Dictionary 1777 (28th ed. 2006), which are paired air-filled cavities in the bones of the face lined by mucous membranes, id. at 1776. Balloon sinuplasty is offered as a less invasive surgical treatment for sinusitis than traditional endoscopic sinus surgery, which involves removal of tissue and bone.

uninflated, into the ethmoid sinus cavity by means of an access probe. Once in situ, the balloon could be inflated by injecting a substance into it through the catheter. When the balloon was filled in this way with Kenalog, the steroid would gradually diffuse out of the pores and bathe the ethmoid cavity over a roughly two-week period. The size of the pores had been calibrated to Kenalog's viscosity to achieve this result. Indeed, the SAB discussed the importance of fine-tuning the pore size to ensure that, when inflated with Kenalog specifically, the steroid would not leak out of the balloon too quickly.

2. Regulatory history of Stratus

Although the Stratus device was designed for use in treating ethmoid sinusitis by delivering Kenalog to the ethmoid sinuses, the SAB and the project team, with Facteau's approval, decided to pursue a regulatory strategy of first gaining § 510(k) clearance for the device for use as a post-surgical spacer capable of releasing saline, and later seeking a second § 510(k) clearance for use as a system to deliver Kenalog to the ethmoid sinuses.

In line with this strategy, Acclarent filed a premarket notification in August 2006, seeking § 510(k) clearance to market Stratus for use "as a postoperative spacer to maintain an opening to the ethmoid sinus within the first 14 days following surgery" and to "help[] to prevent obstruction." Acclarent's submission identified the Rains Frontal Sinus Stent as the predicate device.

That device, which Acclarent stated was "substantially equivalent" to Stratus "in indications for use and technological characteristics," is a spacer designed to minimize the post-operative formation of adhesions in the frontal sinus by maintaining an opening in the frontal sinus in the days following surgery. In addition to use as a similar post-operative spacer in the ethmoid sinuses, Acclarent's submitted "Instructions for Use" for Stratus contemplated that, after the device had been inserted into the patient's ethmoid sinuses, the user would inject saline through the catheter into the perforated balloon and, after trimming away the catheter shaft, leave the device in place for up to fourteen days to "allow[] saline to moisten the [surrounding] area." In September 2006, the FDA cleared Stratus for the use indicated in Acclarent's premarket notification.

Although Acclarent's § 510(k) submission specifically contemplated that Stratus would be used with saline to moisten the ethmoid sinuses, it was understood by the SAB that 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. Rather, when injected, saline would rapidly flow out. The amount of saline that could fit in the Stratus balloon was also too small to be of much therapeutic value.

Consistent with Acclarent's two-step regulatory strategy, it wrote to the FDA in April 2007 seeking to change

Stratus's labeling to add an indication to use Stratus "to irrigate the sinus space for diagnostic and therapeutic procedures." Acclarent also 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.

The following month, the FDA denied Acclarent's request. The FDA sent a letter to Acclarent communicating that the proposed use of Stratus with a therapeutic agent might render it a drug-device "combination product" under 21 C.F.R. § 3.2(e), and hence subject to review both as a drug and as a device. The letter also made clear that, even if the use of Stratus with a therapeutic agent did not render it a combination product, the proposed changes to the device's indications for use signaled a significant change or modification in the intended use of the device such that Acclarent would "need to submit a new 510(k)" and receive FDA clearance "prior to marketing [Stratus]" with the proposed changes in intended use.

Notwithstanding this setback, in September 2007, with Facteau and Fabian in attendance, the steering committee tasked with developing and commercializing Stratus approved a proposal to market Stratus as a product to deliver Kenalog to the ethmoid sinuses, with plans for a commercial launch in the third or fourth quarter of 2008. The committee recognized that for a commercial launch, Acclarent needed -- but lacked -- regulatory approval for

Stratus's use with a drug delivery indication. To that end, the committee made plans to submit a premarket notification seeking § 510(k) clearance to market Stratus for drug-delivery use, with the first quarter of 2008 as an optimistic target timeline.

By November 2007, Acclarent had concluded that a successful § 510(k) submission for Stratus to be used for drug delivery purposes would need to be supported by appropriate clinical studies. But the clinical study Acclarent was conducting had to be halted when, in December 2007, the FDA determined that it posed a significant risk to its subjects. To proceed, Acclarent needed to submit a proposal for a new study for the FDA's approval. Although the FDA approved a new study in August 2008, it too was halted -- in July 2009 -- after reports of adverse events. Ultimately, Acclarent never completed an approved study to support Stratus's use with Kenalog and thus never filed a premarket notification for that intended use.

3. Stratus Enters the Market

Despite the lack of § 510(k) clearance for Stratus to be used with Kenalog, Acclarent proceeded with the plan to begin marketing the device for that use in the second half of 2008. With Facteau's approval, Acclarent promoted Stratus for use with Kenalog at the July 2008 meeting of the Sinus Forum, an annual conference fully sponsored at the time by Acclarent, which Facteau and Fabian both attended. One panel session featured, via video

feed, live demonstrations of Stratus by two surgeons, Dr. Douglas Hoisington and Dr. Michael Friedman, whose display included filling the balloon with Kenalog. The panel members explained how Stratus was designed to allow Kenalog to escape gradually into the ethmoid cavity while the device was in situ. Hoisington, a member of Acclarent's SAB, also indicated that Stratus was not suited for its cleared use by demonstrating how saline solution would immediately run out of the device upon injection. Hoisington explained that the perforations in the balloon were designed to be small enough so that Kenalog, a more viscous fluid, would seep out slowly. This live demonstration of Stratus was included in the 2008 Sinus Forum at Facteau's direction. Facteau's goal was to showcase Stratus's use with Kenalog, although Hoisington and Friedman themselves made the ultimate decisions to go ahead with their demonstrations.

Around this time, Acclarent also began commercially distributing Stratus on a limited market release, selling the device on a trial basis within a small number of sales territories and to a select group of doctors. The limited launch of Stratus was a commercial success. Acclarent's management therefore decided to expand the marketing of Stratus to all potential customers. Leading up to this full commercial launch, Facteau emailed several members of the SAB with a slide presentation on how Stratus would be commercially positioned. The presentation

described Stratus as "simply a way to obtain sustained drug delivery to [a] targeted sinus or sinus complex." In this period, Facteau and Fabian also participated in a conference call with some of Acclarent's sales and training personnel, during which Facteau spoke about presenting Stratus to ENT surgeons as a way of delivering Kenalog to the ethmoid sinuses.

Acclarent launched Stratus for full commercial distribution at the 2008 meeting of the American Academy of Otolaryngologists and American Rhinologic Society ("AAO conference"), which took place in September 2008. As the annual meeting of the major professional organization for ENT surgeons, the AAO conference provides an opportunity for device manufacturers to set up booths to exhibit their products and share information about these products with potential customers. Acclarent's booth was divided into two sides, one staffed by sales representatives focused on selling to the U.S. market, the other by representatives focused on the international market. As directed by Acclarent regulatory officers, representatives on the U.S. side refrained from discussing off-label uses for Stratus, although the U.S.-side representatives also did not discuss or demonstrate Stratus for use as a spacer with saline. U.S.-side representatives were instructed to send attendees who asked about the uses for Stratus to the international side. The international-

side representatives would then share information about using Stratus for delivering Kenalog.

4. Internal Training of Sales Representatives

Acclarent required newly hired sales representatives to complete a month-long training program, including two weeks of on-site training, where they would learn how to promote Stratus and other Acclarent products. Fabian led some of the training sessions and generally attended throughout to supervise. Facteau also spoke and gave a presentation at some of these sessions. Trainees were taught how to present Stratus to ENT surgeons who were potential customers for the product by describing Stratus's features and benefits and how to operate it.

The sales training staff and other presenters repeatedly conveyed to new hires that Stratus was designed to be used, and was expected to be used by most surgeons, to deliver Kenalog. Trainees were not taught about any clinical benefit that Stratus could provide when used as a spacer with saline, and they were trained to tell surgeons that although Stratus was cleared for use in the United States only as a spacer with saline, it was approved for use with Kenalog in Europe. In addition, new hires were advised to ask surgeons "probing" or leading questions that would

prompt the surgeons to inquire about Stratus's potential use for steroid delivery to the sinuses.[6]

Acclarent also provided sales representatives with a document -- reviewed and approved by Acclarent officers including Fabian -- to guide them in discussing Stratus with potential customers and to "help them understand what they can and can't say about . . . Stratus" and its intended use. This "physician discussion guide" recommended that sales representatives tell surgeons that, although Stratus was cleared only for use with saline, Acclarent "expect[ed]" that some surgeons "may want to infuse the device with a therapeutic fluid, steroid, antibiotic, antifungal, instead of saline." The guide also noted that "the only agent that works optimally with [Stratus] is [Kenalog]." By contrast, the guide provided no suggestions on how to explain the clinical benefit of using Stratus to deliver saline. The guide also included "probing questions" that sales representatives might use to invite inquiries from surgeons about using Stratus with Kenalog.

[6] Facteau maintains that this training was properly designed to allow sales representatives to discuss using Stratus with Kenalog while remaining within the FDA's safe-harbor policy, which excludes manufacturer communications about off-label use of products from being considered evidence of a new intended use if those communications occur in response to unsolicited inquiries from health care professionals. See infra Section II.A.

Particularly successful sales representatives were invited by the sales team management, including Fabian, to share their sales techniques and marketing materials with other representatives. The promotional slide presentation for Stratus used by one such top-performing sales representative, Jason Elmore, was widely shared in this way. This presentation described Stratus as "designed to elute Kenalog-40," that is, designed to allow the steroid to diffuse gradually out of the device.

5. Promoting Stratus for Sale

The Acclarent sales representatives who testified at trial reported that they were never given marketing materials for Stratus that described benefits from using the device as a spacer with saline. By contrast, Acclarent made available a video for representatives to use in their pitches that depicted a surgeon implanting Stratus and filling the balloon with Kenalog. Acclarent also provided "sell sheets" -- reviewed and approved by Fabian -- that sales representatives could use in pitching Stratus. These sell sheets included a picture of Stratus that appeared to show the balloon filled with Kenalog.

The Acclarent sales representatives who testified about how they promoted Stratus to their customers uniformly stated that their pitches positioned Stratus as a device to deliver Kenalog, rather than as a spacer with saline. This testimony was corroborated by testimony from multiple ENT surgeons who had been

approached by Acclarent sales representatives about Stratus. The surgeons testified that the sales pitches they received positioned Stratus as a device for delivering Kenalog, not for use as a spacer with saline.

These sales pitches bore abundant fruit. From 2008, when Stratus was brought to market, until 2011, the final year appellants were employed at Acclarent, the gross revenue Acclarent earned from sales of Stratus totaled $33.5 million.

6. Training for Surgeons Who Bought Stratus

Acclarent provided training on how to use Stratus for the surgeons who ordered the device. The training sessions featured both slide presentations and a laboratory-based segment where participating surgeons had the opportunity to practice using the technology with cadaver heads or anatomically correct model heads. Although the Acclarent trainers would inform participating surgeons that Stratus was cleared for use as a spacer with saline, the slide presentations did not describe how to use Stratus for its cleared use. They did, however, tell surgeons how to use Stratus with Kenalog. For example, one slide in the standard deck used for these training presentations featured a depiction of Stratus with the balloon filled with Kenalog. Fabian reviewed and approved this slide deck. During the laboratory-based segment of the training sessions, participating surgeons would usually learn

to use Stratus by filling the balloon with Kenalog or coffee creamer, a substance that looks like the steroid.[7]

In line with this training and the sales pitches they received from Acclarent's sales representatives, the surgeons who bought Stratus predominantly used it off-label to deliver Kenalog or some other drug. Acclarent was aware that Stratus was predominantly being used off-label since it notified the FDA of this fact in a March 2010 letter.[8]

C. Procedural History

In April 2015, a grand jury returned an eighteen-count indictment against Facteau and Fabian. In addition to counts alleging conspiracy, securities fraud, and wire fraud, the indictment included ten counts specifically directed to the unlawful off-label promotion of Stratus. Five counts charged appellants with commercially distributing an adulterated device with the intent to defraud and mislead in connection with five shipments of Stratus between October 2009 and February 2011. See

[7] Saline solution, by contrast, is clear.

[8] The Acclarent sales representatives who testified all reported that they only knew of surgeons who used the device with Kenalog and were aware of no surgeons who used it with saline. The record, however, does contain evidence of at least one doctor who used Stratus for its cleared use. Dr. Hoisington, a member of the Acclarent SAB, testified that he used Stratus as a post-operative spacer with saline in about 15 percent of the procedures he performed with the device. At other times, he used Stratus with an antifungal solution, an antibiotic solution, or Kenalog. Hoisington's most common use for Stratus was to deliver Kenalog.

21 U.S.C. §§ 331(a), 333(a)(1)-(2), 351(f)(1)(B). Another five counts charged them with commercially distributing a misbranded device with the intent to defraud and mislead in connection with five other shipments of Stratus between December 2009 and May 2011. See id. §§ 331(a), 333(a)(1)-(2), 352(a), 352(f), 352(o). The charges for distributing a misbranded device alleged three theories of misbranding: false and misleading labeling, in violation of § 352(a); inadequate directions for use, in violation of § 352(f); and failure to file a required premarket notification, in violation of § 352(o). The securities fraud charges and one wire-fraud count were dismissed on the government's motion before trial.

After a thirty-day trial spanning June and July 2016, the jury acquitted Facteau and Fabian of the conspiracy and remaining wire fraud counts but returned guilty verdicts on all ten counts charging them with distribution of an adulterated and misbranded device.[9] However, the jury found that appellants had not committed those violations with the intent to defraud or mislead, thus finding them guilty only of the misdemeanor form of the offenses.

[9] With regard to the misbranding counts, the jury found that the government had proven misbranding for lack of regulatory clearance but had not proven its theories based on false or misleading labeling or inadequate directions for use.

In August 2016, appellants jointly moved for judgments of acquittal. See Fed. R. Crim. P. 29(c). In challenging their convictions, appellants raised five claims relevant to this appeal: (1) their convictions were based on truthful, non-misleading speech, thereby infringing their rights under the First Amendment; (2) the regulatory scheme under which they were convicted is unconstitutionally vague; (3) the jury was improperly instructed on the evidence that may be considered in determining a device's intended use; (4) they lacked fair notice of the case against them, and thus were denied due process, because the government proceeded on a novel prosecutorial theory and relied on internal company communications as evidence of intended use; and (5) the government presented insufficient evidence of statements promoting off-label use made by them or by Acclarent employees with respect to the ten shipments of Stratus that grounded their convictions.

Rejecting these and other claims, the district court denied appellants' motion in September 2020. The court subsequently imposed a $1 million fine on Facteau and a $500,000 fine on Fabian. Appellants' timely appeals followed.

II.

On appeal, Facteau and Fabian reiterate numerous objections to their convictions, with some claims of error raised

jointly and others raised only by one of them.[10] Fabian also challenges the amount of his fine. We begin with appellants' First Amendment claims and then consider in turn their arguments concerning the statutory concept of "intended use."[11] Finally, we address Fabian's remaining claims, which challenge the sufficiency of the evidence and -- based on the Eighth Amendment's Excessive Fines Clause -- his $500,000 penalty.

A. First Amendment Claim

Facteau's First Amendment attack on his conviction takes the form of an instructional challenge. He argues that the district court improperly refused appellants' proposed instruction, which would have prevented the jury from considering any truthful, non-misleading promotional speech as evidence of the intended use of Stratus. Instead, the court instructed the jury that it could consider such speech. Facteau maintains that the court erred for two reasons. First, using promotional speech as evidence of intended use in effect criminalizes that speech, in

[10] Fabian incorporated by reference the arguments asserted in Facteau's brief. See Fed. R. App. P. 28(i). Hence, although for clarity's sake we discuss certain arguments as made by Facteau, our discussion of those arguments applies to both appellants. On the other hand, because Facteau did not join Fabian's brief, our discussion of issues raised by Fabian alone applies only to him.

[11] Fabian argues that as a matter of text and precedent, "intended use" encompasses only promotional speech, and thus the district court's instruction to the contrary was error. Both appellants argue that the government's interpretation of "intended use" violates due process.

contravention of a growing body of law in the Second Circuit holding that truthful, non-misleading speech promoting off-label use is protected. Second, because the FDA has adopted a policy that shields certain non-promotional speech from evidentiary use, allowing speech outside of this safe harbor to serve as evidence imposes an impermissible content-based burden on "disfavored" speech, especially off-label promotional statements.

After reviewing the district court's instructions and important background First Amendment principles, we consider each of these arguments in turn.

1. Background

At trial, appellants proposed that the court's instructions on the adulteration and misbranding charges include the statement that "truthful, non-misleading statements cannot give rise to a new intended use." The court declined to give that instruction. Instead, it told the jurors that, because "[i]t 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." Nevertheless, the court continued, jurors could 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." Appellants objected to the court's "failure to instruct the jury that truthful speech cannot be considered as evidence of intended use."

2. Legal Analysis

Facteau appears to take issue both with the district court's rejection of appellants' proffered instruction, as well as the instruction the court ultimately delivered to the jury. Where, as here, we consider a preserved claim that the trial court's instruction misstated the law, we review the court's instruction de novo. United States v. Florentino-Rosario, 19 F.4th 530, 534 (1st Cir. 2021). We test whether the district court's refusal to give appellants' requested instruction constituted reversible error by asking if that instruction was "(1) substantively correct as a matter of law, (2) not substantially covered by the charge as rendered, and (3) integral to an important point in the case so that the omission of the instruction seriously impaired the defendant's ability to present his defense." United States v. McLellan, 959 F.3d 442, 467 (1st Cir. 2020) (quoting United States v. Baird, 712 F.3d 623, 628 (1st Cir. 2013)). We review the instruction the trial court did give for whether it was "(1) misleading, unduly complicating, or incorrect as a matter of law; and (2) adversely affected the objecting party's substantial rights." United States v. Figueroa-Lugo, 793 F.3d 179, 191 (1st

Cir. 2015) (quotation marks omitted) (quoting United States v. Stark, 499 F. 3d 72, 79 (1st Cir. 2007)). In the present appeal, the question under both inquiries boils down to whether the district court erred because it should have instructed the jurors that they could not consider promotional statements as evidence of Stratus's intended use, rather than instructing the jurors that they could.

To answer that question, we must note at the outset 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." Wisconsin v. Mitchell, 508 U.S. 476, 489 (1993). In Mitchell, the Court held that an aggravated battery defendant's First Amendment rights were not violated by using his statements to prove the racial motive that made him eligible for a sentence enhancement. See id. at 489-90. In reaching that conclusion, the Court did not analyze whether this evidentiary use of the defendant's speech could satisfy some heightened standard of scrutiny. Rather, the Court concluded that there was no First Amendment violation because the use of a defendant's speech as proof of his motive or intent simply does not implicate the First Amendment. Id. at 489.

Facteau's First Amendment argument is in obvious tension with the Court's holding in Mitchell. For the crux of his instructional error claim, he argues that because a manufacturer's

truthful, non-misleading speech promoting the off-label use of a device is protected under the First Amendment, the district court should have instructed the jury that, in effect, it may not consider any such speech as evidence of the device's intended use. To do otherwise, the court's instruction would need to withstand heightened scrutiny, which Facteau argues it could not. But, as indicated, Mitchell makes clear that the First Amendment offers no protection against using otherwise protected speech as evidence of intent or to establish the elements of a crime. Facteau offers two explanations for why the Court's holding in Mitchell does not reach this case, and hence appellants' proposed instruction was compelled by the First Amendment.

i. Whether Using Promotional Speech as Evidence of Intended Use De Facto Criminalizes That Speech

Facteau first argues that the First Amendment does not permit the factfinder here to consider off-label promotional speech as evidence of intended use by pointing to the Second Circuit's decision in United States v. Caronia, 703 F.3d 149 (2d Cir. 2012), and its progeny in Amarin Pharma, Inc. v. FDA, 119 F. Supp. 3d 196 (S.D.N.Y. 2015). In a significant decision limiting, for the first time, the use of off-label promotional speech in the context of misbranding prosecutions, the court in Caronia held that the defendant's conviction violated the First Amendment because the prosecution "repeatedly argued that [he] engaged in

criminal conduct by promoting and marketing the off-label use of . . . an FDA-approved drug," leaving "the jury to understand that [his] speech was itself the proscribed conduct." 703 F.3d at 161. Because it found that the defendant "was prosecuted [for] precisely his speech in aid of pharmaceutical marketing," id. at 162, the court applied heightened scrutiny under Central Hudson Gas & Electric Corp. v. Public Service Commission of New York, 447 U.S. 557 (1980), and concluded that the prosecution did not survive that standard, Caronia, 703 F.3d at 164-69.[12]

Taking his cue from Caronia, Facteau contends that permitting the jury to consider his off-label promotional speech in assessing his guilt under the FDCA amounts to the de facto criminalization of his protected speech, creating a "backdoor" through which the government may sneak past the First Amendment's reach and punish appellants simply for the things they said about Stratus. In Caronia, the government argued, as it does here, that it was merely relying on the defendant's speech as evidence of his intended use for the drug, rather than punishing him for his

[12] Applying Caronia as binding precedent, the district court in Amarin sided with a drug manufacturer in its pre-enforcement challenge against the FDA, declaring that the manufacturer had a First Amendment right to "engage in truthful and non-misleading speech promoting the off-label use of [its product]" and that "such speech may not form the basis of a prosecution for misbranding." 119 F. Supp. 3d at 237.

speech.[13] See 703 F.3d at 160-62. While stressing that its opinion did not question the general principle that speech can constitute evidence of intended use, the Caronia majority was not persuaded that the government's use of speech was limited to evidentiary purposes in that case. Id. It pointed, among other things, to the government's sole reliance on the defendant's statements to establish his criminal liability, the government's profligate use of his statements in its summation to the jury, and the court's jury instructions, which "flatly stated . . . that pharmaceutical representatives are prohibited from engaging in off-label promotion" and "left the jury to understand that Caronia's speech was itself the proscribed conduct." Id. at 161. It also bears emphasis that the defendant in Caronia was a sales representative, whose sole job function was to make promotional statements about the product. Moreover, the government's theory of misbranding focused on the defendant's statements promoting off-label uses and the consequence that the drug's labeling did not bear "adequate directions for use." See 21 U.S.C. § 352(f)(1).

[13] Likewise, in dissent, Judge Livingston posited that the government's reliance on the defendant's speech served no purpose other than as evidence of the drug's intended use, and she pondered whether, under the majority's rule, any prosecution could rely on off-label promotional speech as evidence of the defendant's intended use for a potentially misbranded product. Caronia, 703 F.3d at 172-77.

Though Facteau's reliance on Caronia is understandable, that case is meaningfully different from the one at hand and provides us with no basis to depart from the rule in Mitchell that the evidentiary use of speech does not violate the First Amendment. Unlike in Caronia, the government's case here relied on a wide array of evidence, which included not only promotional speech about off-label uses but also internal communications regarding regulatory and marketing strategy and the product's physical design. It is not the case, as it was in Caronia, that the government set out to punish appellants for what they said about the product; rather, what appellants said about Stratus simply shed light on how they intended it to be used. The district court's instructions made as much clear, specifying 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" and that the jury 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."

Moreover, the government's successful theories for misbranding and adulteration did not turn on whether Acclarent's statements left Stratus without adequate directions for use, as was the case in Caronia. Though the government did present that theory of misbranding to the jury, the jury rejected that approach

and instead found appellants guilty of misbranding because Stratus lacked the proper regulatory clearance -- a theory of misbranding less intertwined with appellants' speech. And, unlike the defendant in Caronia, both Facteau and Fabian were high-level executives at Acclarent responsible not just for what was said about Stratus publicly but also for internal decisions on product design and regulatory strategy (in the case of Facteau), as well as sales strategy (in the case of both).

In short, Caronia does not render appellants' proposed instruction an accurate statement of law that properly captured the nuances of the First Amendment interests at stake in this case. Calculated to cut off any evidentiary use of off-label promotional speech, appellants' preferred instruction would have removed this case from the teachings of Mitchell and placed it within the domain of Caronia without the facts to justify such a move. We discern no error in the district court's refusal to take that step, nor in the instructions it ultimately handed down, which better respected the sensitive balance between protecting promotional speech without shielding such speech from evidentiary value.

In so holding, we note that we are in alignment with our sister circuits -- including the Second. 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. See, e.g., Whitaker v. Thompson, 353

F.3d 947, 953 (D.C. Cir. 2004) (holding that it is "constitutionally permissible" to use a seller's claims as evidence of intended use, even when doing so "renders [the] otherwise permissible act [of selling the product with FDA approval] unlawful"); Nicopure Labs, LLC v. FDA, 944 F.3d 267, 282 (D.C. Cir. 2019) (reaffirming Whitaker); United States v. LeBeau, 654 F. App'x 826, 830-31 (7th Cir. 2016). Indeed, as we have noted, the Caronia court assumed that evidentiary use of statements to prove FDCA violations would be permissible under the First Amendment but concluded on the facts that the prosecution did not use speech in that way. See 703 F.3d at 161. See also U.S. ex rel. Polansky v. Pfizer, Inc., 822 F.3d 613, 615 n.2 (2d Cir. 2016) ("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.").

We find relevant and persuasive this consistent authority from other circuits that the First Amendment is not implicated by the evidentiary use of truthful, non-misleading promotional speech to establish a drug's intended use to obtain a conviction under the FDCA. Appellants' convictions fall soundly within that domain. The trial court did not criminalize appellants' speech itself, instructing the jury to consider promotional speech only insofar as it shed light on appellants'

intended use for Stratus. Accordingly, Facteau's reliance on Caronia fails.

ii. Whether the FDA's Safe Harbor Policy Subjects Promotional Speech to a Discriminatory Burden

Facteau's additional First Amendment argument targets FDA guidance explaining when truthful, non-misleading speech regarding off-label uses will not be considered evidence of a product's intended use. In Facteau's telling, this "safe harbor" draws content-based distinctions between favored and disfavored speech, burdening speech that affirmatively promotes an off-label use of a device -- by considering it as evidence of intended use -- while excluding evidentiary uses of science-based responses to unsolicited questions from physicians regarding off-label use and the distribution of certain scientific literature. He contends further that, because these burdens are content- and viewpoint-based, they cannot survive heightened scrutiny and therefore violate the First Amendment.

Facteau's argument draws upon Supreme Court precedent recognizing that policies singling out certain speech for regulatory burdens -- based on the content of that speech -- are subject to heightened judicial scrutiny. See, e.g., Sorrell v. IMS Health Inc., 564 U.S. 552, 565 (2011) (holding that a law "designed to impose a specific, content-based burden on protected expression" is subject to "heightened judicial scrutiny"); United

States v. Playboy Ent. Grp., Inc., 529 U.S. 803, 812 (2000) ("[C]ontent-based burdens must satisfy the same rigorous scrutiny as . . . content-based bans."). In Sorrell, for instance, the Court held unconstitutional a Vermont law that required pharmaceutical marketers to obtain a physician's consent before they could use data about his prescribing practices to inform their marketing strategy but imposed no similar requirement on using that data for other purposes, such as for research or patient education. See 564 U.S. at 559-60, 565. Facteau contends that the FDA's safe harbor operates in similar fashion by using the content of a medical product manufacturer's speech to determine whether that speech will bear the burden of potentially being used as evidence of intended use.

We understand Facteau's theory to fit into his First Amendment instructional error claim by supplying another rationale for the correctness of appellants' rejected instruction, even though seemingly out of step with Mitchell, in the context of this case. Although it is generally permissible for a jury to consider promotional speech as evidence of intent, any evidence so presented to the jury because it is not protected by the safe harbor would be the product of a government policy that unequally foists the burden of potential evidentiary use upon certain speech based on its content. Thus, the court should have instructed the jury to

exclude all evidence derived from appellants' promotional speech, as appellants requested.

The government asserts that this argument is forfeited because it was not raised below. We agree. Although appellants made general First Amendment objections to the court's instruction that the jurors may consider promotional speech as evidence of intent, and at times couched their arguments in terms of content- and viewpoint-based discrimination, they never suggested that the FDA's safe-harbor guidance constituted such discrimination. Indeed, Facteau's trial counsel insisted -- over the government's objection -- that the court adopt an instruction modeled on one of the guidance documents, hardly suggesting that appellants viewed the safe harbor as odious to protected speech.[14] Because "a party is not at liberty to articulate specific arguments for the first time on appeal simply because the general issue was before the district court," United States v. Slade, 980 F.2d 27, 31 (1st

[14] We recognize that Facteau's counsel requested this instruction as a "fallback" after the trial court rejected appellants' view that any consideration of truthful, non-misleading statements to show improper intent violated the First Amendment. Nonetheless, Facteau's counsel expressly agreed that appellants were "not objecting to this instruction as-is over and beyond the views they already have of the First Amendment in this case," thereby disclaiming any First Amendment argument beyond their objection rooted in Caronia.

Cir. 1992), we will apply plain error review to assess Facteau's unpreserved argument.[15]

Under that standard, Facteau "must show '(1) that an error occurred (2) which was clear or obvious and which not only (3) affected [his] substantial rights, but also (4) seriously impaired the fairness, integrity, or public reputation of judicial proceedings.'" United States v. Nieves-Meléndez, 58 F.4th 569, 579 (1st Cir. 2023) (quoting United States v. Merced-García, 24 F.4th 76, 79-80 (1st Cir. 2022)). An error is only clear or obvious when it is "'indisputable' in light of controlling law." Merced-García, 24 F.4th at 80 (quoting United States v. Rabb, 5 F.4th 95, 101 (1st Cir. 2021)); see also United States v. Grullon, 996 F.3d 21, 33 (1st Cir. 2021) ("[P]lain error cannot be found . . . absent clear and binding precedent." (quoting United States v. Marcano, 525 F.3d 72, 74 (1st Cir. 2008) (per curiam))).

[15] At times, Facteau's briefing regarding this additional First Amendment argument appears to stray from the framing of an instructional challenge, engaging instead in a more fundamental and broad-based attack on the FDA's safe harbor policy. But Facteau never presented any such argument to the district court and does not suggest before us how the safe harbor policy concretely affected his prosecution beyond the conclusory assertion that "[t]he government's . . . enforcement approach improperly affected every aspect of the trial here." Accordingly, we would deem any such theory waived. See United States v. Zannino, 895 F.2d 1, 17 (1990) ("[I]ssues adverted to in a perfunctory manner, unaccompanied by some effort at developed argumentation, are deemed waived."). Instead, we construe Facteau's argument as part of his primary instructional error challenge, reviewable for plain error.

Facteau principally points to two guidance documents issued by the FDA -- a draft document from 2011 ("2011 guidance") and a revised draft from 2014 ("2014 guidance") -- as the source of the safe harbor policy that, he urges, results in a burden on the speech excluded from the safe harbor by subjecting only such "disfavored" speech to the peril of being used as evidence of intended use.[16] The 2011 guidance sets out standards for how manufacturers should respond to unsolicited requests for information about off-label uses for their devices. See U.S. Food & Drug Admin., Draft Guidance for Industry Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices (2011). For example, the 2011 guidance recommended that manufacturers respond to such requests with "non-biased information or data" concerning the off-label use. Id. at 8. The 2011 guidance also recommended that responses to unsolicited requests be generated by scientific personnel rather

[16] Facteau also cursorily mentions, as among the safe harbor guidance that he claims imposes a First Amendment-violative burden on speech, a 2009 FDA guidance document on recommended practices for the distribution of medical or scientific publications discussing off-label uses of drugs or devices, as well as a notice by the FDA regarding Washington Legal Foundation v. Henney, 202 F.3d 331 (D.C. Cir. 2000). See U.S. Food & Drug Admin., Guidance for Industry: Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (2009); U.S. Food & Drug Admin., Decision in Wash. Legal Found. v. Henney, 65 Fed. Reg. 14,286 (Mar. 16, 2000).

than by sales or marketing personnel. Id. at 8-9. If a manufacturer abided by these standards, the 2011 guidance announced, the FDA would not use the manufacturer's response as evidence of a new intended use. Id. at 9.

The 2014 guidance articulated standards governing manufacturers' dissemination of scientific and medical publications discussing off-label uses to health care professionals and entities. See U.S. Food & Drug Admin., Revised Draft Guidance for Industry: Distributing Scientific and Medical Publications on Unapproved New Uses — Recommended Practice (2014). The 2014 guidance stated that, if a manufacturer follows these standards, the FDA would not use its distribution of scientific and medical publications discussing off-label use of a device as evidence of a new intended use. Id. at 6.

Facteau devotes much of his briefing to establishing that the FDA's safe harbor amounts to content-based discrimination that cannot withstand heightened scrutiny. But this argument depends upon the premise that speech outside of the safe harbor -- and thus subject to potential evidentiary use -- suffers a "burden" raising First Amendment concerns in the first place. On plain error review we must satisfy ourselves that this threshold assertion is "'indisputable' in light of controlling law." Merced-García, 24 F.4th at 80 (quoting Rabb, 5 F.4th at 101). That is a tall order, considering the clarity with which Mitchell

establishes that using speech as evidence ordinarily does not run afoul of the First Amendment. Because Facteau's argument fails to clear the threshold hurdle of demonstrating that the safe harbor policy "burdens" protected speech within the meaning of the First Amendment, we need not analyze whether the safe harbor policy imposes such a burden by drawing content-based distinctions or whether those distinctions would satisfy heightened scrutiny.

To start, Facteau's argument fundamentally misconstrues the nature of the FDA's safe harbor. Far from burdening what device manufacturers may say, the safe harbor guidance expands, rather than contracts, the domain of speech that the government shields from being used as evidence. If, as a general matter, the evidentiary use of speech discussing off-label use does not raise First Amendment concerns, then presumably a policy that limits the consideration of such speech as evidence of intended use does not raise First Amendment concerns either.[17]

Neither of the cases upon which Facteau relies persuades us otherwise. See Sorrell, 564 U.S. 552; Playboy, 529 U.S. 803. While these cases certainly establish the general principle that

[17] We note, moreover, that it is far from clear that the FDA's safe harbor policies make content-based distinctions on speech. In many cases, such as the 2011 guidance on unsolicited questions about off-label use, it is the circumstances under which a statement arises, and not the content of the statement itself, that determine whether the FDA deems that statement open for evidentiary use.

some regulations on speech impose burdens sufficient to raise First Amendment concerns, they fall far short of the "clear and binding precedent" necessary on plain error review to sustain Facteau's argument that the FDA's safe harbor fits that mold. Grullon, 996 F.3d at 33.

The regulations found to impermissibly burden speech in both Sorrell and Playboy took much more direct aim at protected speech -- and imposed far more onerous restrictions on it -- than does the FDA's safe harbor, even in Facteau's telling. The law challenged in Sorrell prohibited pharmaceutical sellers from using, or even receiving, information about doctors' prescribing practices to inform their sales pitches. 564 U.S. at 564-66. In Playboy, a regulation aimed at preventing broadcasts of adult entertainment from reaching children produced a sweeping partial ban of such programming except during late evening hours. 529 U.S. at 811-15.

By contrast, at most, the FDA's safe harbor puts the sellers of medical products on notice about which of their statements the government deems most probative of that product's intended use.[18] That is no different than how a defendant's speech

[18] Facteau assumes that all off-label speech, whether within the safe harbor or otherwise, has equal potential to be probative of intended use. But that assumption defies the common sense behind the FDA's safe harbor policy, which reflects the agency's judgment about the circumstances in which a device seller's off-label speech is more indicative of its state of mind than other

may be probative of the racial animus behind an assault, see Mitchell, 508 U.S. at 489, or soldiers "announcing their sexual orientation" was probative of whether they had violated "Don't Ask, Don't Tell" prior to its repeal, see Cook v. Gates, 528 F.3d 42, 62-64 (1st Cir. 2008). As we have noted, if the FDA's safe harbor marks a departure from the Mitchell baseline at all, it is only because it removes certain speech from government scrutiny, rather than heaping more scrutiny upon the speech that falls outside the safe harbor.

It is of course true that medical device sellers, aware that their speech may become evidence of intended use, will necessarily choose their words carefully when promoting their products. But such efforts do not amount to a "burden" on free expression when it is conduct -- in this case, introducing misbranded or adulterated devices into commerce -- and not speech that the law aims to control. We have said that such "incidental effects" on speech arising from laws directed at non-speech conduct "do[] not . . . implicate the First Amendment." Wirzburger v. Galvin, 412 F.3d 271, 278 (1st Cir. 2005) (citing Arcara v. Cloud

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instances of speech. For instance, the FDA's 2011 draft guidance distinguishes between requests for off-label information that are "solicited" versus "unsolicited." When a physician or patient comes to a manufacturer unbidden and asks about the off-label application of a product, nothing about a manufacturer responding truthfully inherently suggests that it intends the product to be used off-label.

Books, Inc., 478 U.S. 697, 698 (1986)). See also Cook, 528 F.3d at 63 (use of speech as evidence of violation of law "aimed at eliminating certain conduct . . ., not at restricting speech," does not burden speech).

We thus find no merit in Facteau's apparent contention that, because the FDA's safe harbor policy shields some speech from evidentiary use, the jury should have been instructed to disregard all promotional speech as evidence of intended use. And, having rejected the Caronia argument as well, we conclude that Facteau's First Amendment arguments fail to support departing from Mitchell's longstanding rule that using speech as evidence of intent does not implicate the First Amendment. Accordingly, neither the district court's rejection of appellants' proposed instruction nor its decision to instead instruct the jury that it could consider speech for evidentiary purposes was in error.

B. Instructional Error Claim Regarding "Intended Use"

Having decided that the First Amendment poses no obstacle to the government's evidentiary use of appellants' off-label promotional speech, we turn now to Fabian's countervailing argument that the jury should have been instructed that it may consider only such evidence to determine a product's intended use.

1. Background

At the pre-trial charge conference, appellants' counsel objected to the district court's proposed instructions on "intended use" on the ground that those instructions did not convey to the jury that when the government alleges that a medical device serves an intended use for which it has not been approved, that "intended use must be based only on external promotional conduct." Appellants asked the court to instead instruct the jury that only statements made to potential customers bear on a device's "intended use" and that the jurors therefore should not consider internal company documents and communications, responses to doctor-initiated inquiries, and scientific information disseminated in academic and educational venues in evaluating the question of "intended use."

The court declined to give appellants' requested instruction and rejected their challenge to its own instruction. It thus instructed the jury as follows on how a device's "intended use" is to be determined outside of the § 510(k) process:

> The term "intended use" refers to the objective intent of the manufacturer or seller of the device. The intent is determined by such person's expressions or may be shown by the circumstances surrounding the distribution of the device. This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives. It 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. . . .
>
> Mere knowledge that doctors are using a device for purposes other than its labeled use does not give rise to a new intended use. Off-label promotional statements can constitute evidence of an intended use, although truthful, non-misleading speech alone cannot be the basis for a criminal conviction. . . .

After the court charged the jury, appellants objected to the court's "failure to instruct the jury that in determining intended use, the jury must look solely to the external promotional activities surrounding the distribution of a device." Appellants renewed this instructional challenge in their motion for judgments of acquittal.

In ruling on appellants' motion, the district court gave two reasons for rejecting this instructional challenge. First, the instruction as given was consistent with the plain language of the description of "intended use" set out in 21 C.F.R. § 801.4. Second, the position stated in appellants' requested instruction -- that the only relevant evidence of a device's intended use is the manufacturer or seller's external promotional statements -- finds no support in caselaw.

2. Legal Analysis

On appeal, Fabian reiterates his claim that the district court's instruction was legally erroneous and that the court should

have instead instructed the jury that only external promotional statements could be considered in determining whether Stratus was being improperly marketed for a new intended use. Fabian relies first on the definition of "intended use" in § 801.4, which refers to the "objective intent" of the labelers of the device. He claims that reference necessarily limits the focus to external marketing and promotional statements. Fabian also relies on what he asserts are prior judicial interpretations of "intended use" that define that term to encompass only promotional statements communicated to potential customers.

This preserved instructional claim thus requires us to determine whether Fabian's proposed instruction or the contrary instruction given by the district court properly stated the relevant law. Accordingly, our review is de novo. See Florentino-Rosario, 19 F.4th at 534.[19]

Fabian's argument based on the definition of "intended use" in 21 C.F.R. § 801.4 is easily dispatched. As the district court persuasively reasoned, the concept of "objective intent" simply means that there must be "outward expressions" of such

[19] The government argues that we should apply plain error review because Fabian did not specifically object to the district court's failure to give his requested instruction after the court charged the jury. See United States v. Pérez-Rodríguez, 13 F.4th 1, 16 (1st Cir. 2021). The government, however, is mistaken. Fabian did object to the court's refusal to instruct the jury that intended use is to be determined solely by reference to external promotional statements.

intent and not merely "unexpressed thoughts" within the mind of an individual. United States v. Facteau, No. 15-cr-10076-ADB, 2020 WL 5517573, at *17 (D. Mass. Sept. 14, 2020). This notion of intent, which judges a person's mental state by its outward manifestations through speech and conduct, is a familiar concept in the law. See, e.g., Restatement (Second) of Contracts § 18 cmt. a (Am. L. Inst. 1981) ("Assent to the formation of an informal contract is operative only to the extent that it is manifested."). Communications and conduct internal to Acclarent's operations were not any less "objective" because they were not directed at potential customers for Stratus or at the public in general.

Moreover, as the district court noted, the plain text of the then-current version of § 801.4 did not limit relevant manifestations of "objective intent" in the way that Fabian suggests. The regulation stated that objective intent may be shown by "expressions" such as "oral or written statements by [labelers] or their representatives," with no indication that these statements must be directed to individuals outside the company. The regulation also embraced, as a manifestation of "objective intent," "the circumstances surrounding the distribution" of a device -- including evidence that the device was, "with the knowledge of [labelers] or their representatives, offered and used for a purpose for which it is neither labeled nor advertised." Thus, the regulation expressly contemplated that a labeler's

"objective intent" -- and hence a device's intended use -- could be proven with evidence beyond the external promotional statements of a device manufacturer's officers and employees.

Fabian's argument from precedent is equally unavailing. Neither of the out-of-circuit cases he highlights stand for the principle on which he relies, namely that only public-facing promotional statements can provide evidence of a device's intended use. Indeed, in United States v. Articles of Drug for Veterinary Use, 50 F.3d 497 (8th Cir. 1995), the Eighth Circuit expressly held that a seller's "intended application" of a product -- in that case, a suspected adulterated new animal drug -- may be determined by reference to evidence from "any relevant source," including, but not limited to, external promotional statements. Id. at 499-500. To be sure, promotional statements proved exceptionally relevant in that case as the facts centered on literature accompanying the product, see id. at 499-500, but the court did not purport to hold that only such promotional material is probative of the intended use of a product regulated by the FDCA.

The Fourth Circuit's decision in Brown & Williamson Tobacco Corp. v. FDA, 153 F.3d 155 (4th Cir. 1998), is similarly unhelpful to Fabian. Although the panel observed that "no court has ever found that a product is 'intended for use' [as a drug or device] . . . absent manufacturer claims as to that product's

use," id. at 163 (quoting Coyne Beahm, Inc. v. FDA, 966 F. Supp. 1374, 1390 (M.D.N.C. 1997)), the decision does not support Fabian's view that a court may not consider other sources of evidence. Rather, the case merely reinforces the obvious point that labeling and external statements are important sources to consider.

Moreover, Fabian's position is contradicted by other precedent, including from our own court. We long ago stated that, in determining a product's intended use for purposes of a misbranding conviction, courts are "free to look to all relevant sources in order [to] ascertain . . . 'intended use.'" V.E. Irons, Inc. v. United States, 244 F.2d 34, 44 (1st Cir. 1957) (emphasis added). While the specific sources we relied on in V.E. Irons were the literature distributed and the oral representations made in connection with the sale of the misbranded drugs, we did not thereby imply any limitation on the "all relevant sources" standard we announced.

This broad standard has been endorsed by multiple other circuits. For instance, the Federal Circuit, in Allergan, Inc. v. Athena Cosmetics, Inc., 738 F.3d 1350 (Fed. Cir. 2013), stated that the intended use of a product "may be 'derived or inferred from labeling, promotional material, advertising, or any other relevant source.'" Id. at 1357 (quoting United States v. Storage Spaces Designated Nos. 8 and 49 Located at 277 East Douglas, 777 F.2d 1363, 1366 (9th Cir. 1985)). The court expressly "disagree[d]

with [the defendant] that the only relevant evidence is labeling and marketing," and it considered the company's internal "training of resellers" when analyzing the question of objective intent. Id. Similarly, in United States v. An Article of Device, 731 F.2d 1253, 1257 (7th Cir. 1984), the Seventh Circuit determined that a chiropractic instrument was intended to be used as a medical device by examining the instructions that accompanied the device, the "financial arrangements through which chiropractors were trained in the use of the [device]," and testimony from chiropractors about how they used it. See also Action on Smoking & Health v. Harris, 655 F.2d 236, 239 (D.C. Cir. 1980) ("[I]t is well established that the 'intended use' of a product, within the meaning of the [FDCA], is determined from its label, accompanying labeling, promotional claims, advertising, and any other relevant source." (Internal quotation marks omitted) (emphasis added)); United States v. An Article . . . Consisting of 216 Cartoned Bottles, More or Less, Sudden Change, 409 F.2d 734, 739 (2d Cir. 1969) ("It is well settled that the intended use of a product may be determined from its label, accompanying labeling, promotional material, advertising and any other relevant source." (Emphasis added)).

In sum, we do not find Fabian's proposed understanding of "intended use" under § 801.4 persuasive, and we discern no error in the district court's interpretation of that term as stated in

its instruction to the jury. Accordingly, Fabian's instructional challenge fails.

C. Due Process Claims Regarding "Intended Use"

Both Facteau and Fabian contend that their convictions were obtained in violation of the Fifth Amendment's Due Process Clause because "intended use," as that term is used in the relevant FDCA provisions and accompanying regulations, is unconstitutionally vague. Facteau makes a further due process claim that, because the government and courts at the time of his conduct took the position that only external marketing statements promoting off-label use can be considered as evidence of a new intended use, his prosecution under a novel and more expansive interpretation of intended use denied him the fair notice required by due process.

Appellants raised both due process claims in the district court, and we therefore review them de novo. See United States v. Silva, 794 F.3d 173, 177 (1st Cir. 2015).

1. Unconstitutional Vagueness Claim

The government violates the Due Process Clause if it "tak[es] away someone's life, liberty, or property under a criminal law so vague that it fails to give ordinary people fair notice of the conduct it punishes, or so standardless that it invites arbitrary enforcement." Johnson v. United States, 576 U.S. 591, 595 (2015) (citing Kolender v. Lawson, 461 U.S. 352, 357-58

(1983)); accord Frese v. Formella, 53 F.4th 1, 6 (1st Cir. 2022) (identifying "lack of notice" and the prospect of "discriminatory enforcement" as the hallmarks of an unconstitutionally vague statute). In most contexts, the test for unconstitutional vagueness is whether the challenged law is so indefinite that it "fails to provide a person of ordinary intelligence fair notice of what is prohibited." Frese, 53 F.4th at 6 (quoting United States v. Williams, 553 U.S. 285, 304 (2008)). For provisions that concern economic regulation, however, the test is whether a "business person of ordinary intelligence would understand" what conduct is prohibited -- a "less strict vagueness test." Vill. of Hoffman Ests. v. Flipside, Hoffman Ests., Inc., 455 U.S. 489, 499, 501 (1982) (emphasis added).[20]

Appellants offer two rationales to support their contention that the legal framework under which they were

[20] Courts are less likely to conclude that statutes and regulations "addressed to sophisticated businessmen and corporations" are unconstitutionally vague because of an assumption that, given the "complexity" of economic regulation, such parties "necessarily consult counsel in planning their activities," and some "administrative process" will often be available "to secure advisory interpretations of the statute [or regulation]" at issue. United States v. Lachman, 387 F.3d 42, 57 (1st Cir. 2004). By contrast, vagueness review is more stringent when the challenged laws implicate the First Amendment's protections for speech. See FCC v. Fox Television Stations, Inc., 567 U.S. 239, 253-54 (2012) (noting that a more "rigorous" vagueness inquiry is appropriate "to ensure that ambiguity does not chill protected speech"). As explained above, however, the adulteration and misbranding offenses underlying appellants' convictions do not raise First Amendment concerns.

convicted -- and particularly the term "intended use" -- is so vague as to violate the Due Process Clause. First, they argue that the broad scope of evidence that § 801.4 allows to determine intended use makes the term unconstitutionally vague. Second, they argue that there is a history of inconsistent agency and judicial interpretations of "intended use" that indicates that the term is impermissibly vague. We address each of these arguments in turn.

i. Evidence of "Intended Use" Under § 801.4

Appellants contend that the government's position that a device manufacturer's "intended use" for a device may take into account "'all circumstances' from 'any relevant source' relating to the [device]" -- an interpretation adopted by the district court in its jury instructions -- renders the FDCA provisions underlying their convictions unconstitutionally vague.[21] They argue that, when such a wide array of evidence may be used to

[21] The government does not dispute appellants' depiction of its interpretation of the regulation and, indeed, the record reflects the broad construction they posit. In its closing argument, for example, the government told the jurors that they could "look at all of the circumstances surrounding the distribution of the device to figure out what would be the intended use of the device." As recounted above, the district court's jury instructions also reflected this interpretation. The court told the jurors that the intended use for a device "refers to the objective intent" of the device manufacturer or seller, which intent is "determined by" the manufacturer or seller's "expressions" and "the circumstances surrounding the distribution of the device."

support a finding of "intended use" -- and thus criminal liability -- manufacturers lack fair notice of the conduct prohibited under the adulteration and misbranding offenses, and the government's authority to prosecute violations of those offenses improperly lacks any limiting standards.

The vagueness doctrine is primarily concerned with whether the language of a legal provision is sufficiently clear.[22] Necessarily, then, appellants must show that § 801.4's definition of "intended use" -- which looks to the "objective intent" of the seller as determined by his "oral or written statements" and "the circumstances surrounding the distribution" of the device -- is so unclear that it does not give fair warning of when the seller will be found to have an intended use for their device that differs from the use for which it has been cleared.

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[22] The vagueness doctrine's focus on the language of a penal law is evident from the earliest cases developing the doctrine. See, e.g., Connally v. Gen. Constr. Co., 269 U.S. 385, 391 (1926) ("That the terms of a penal statute creating a new offense must be sufficiently explicit to inform those who are subject to it what conduct on their part will render them liable to its penalties is a well-recognized requirement, . . . and a statute which either forbids or requires the doing of an act in terms so vague that men of common intelligence must necessarily guess at its meaning and differ as to its application violates the first essential of due process of law." (Emphases added)); McBoyle v. United States, 283 U.S. 25, 27 (1931) ("[I]t is reasonable that a fair warning should be given to the world in language that the common world will understand, of what the law intends to do if a certain line is passed. To make the warning fair, so far as possible the line should be clear." (Emphasis added)).

Appellants fail to explain how, as a textual matter, the law lacked sufficient clarity to apprise them of when they would be criminally liable for distributing a device with an unapproved intended use. 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. 21 C.F.R. § 807.81(a)(3)(ii). And, as noted in our discussion of Fabian's instructional-error claim, "objective intent," which § 801.4 relies upon in its definition of "intended use," is a familiar and well-established concept in the law. Indeed, the Supreme Court has indicated that the objective intent standard is sufficiently determinate for purposes of the vagueness doctrine. See Williams, 553 U.S. at 306 (holding that "[w]hether someone . . . had an intent is a true-or-false determination, not a subjective judgment" and hence specifies a sufficiently determinate standard of criminal culpability). Moreover, the regulation goes on to explain that such objective intent may be reflected in a seller's "statements" or other "circumstances surrounding the distribution" of the device. To be sure, the provision casts a wide net. It does so, however, in language that fairly apprises the reader of the broad range of conduct that may reasonably reflect a device's intended use.

Especially given the less stringent vagueness test that applies to economic regulation, appellants have failed to show that "intended use," as that term is defined in § 801.4, is unconstitutionally vague. At most, there may be some uncertainty under § 801.4 about when, in a close case, there will be sufficient evidence to prove that a manufacturer marketed a device for an off-label intended use. That type of uncertainty, however, does not give rise to a valid vagueness claim. As the government points out, a penal law is impermissibly vague when it fails to give "fair notice of what is forbidden," United States v. Morosco, 822 F.3d 1, 5 (1st Cir. 2016), not simply when it may be difficult to determine whether, given the evidence in a particular case, the elements of the offense defined in the law have been proved, see Williams, 553 U.S. at 306 ("What renders a statute vague is not the possibility that it will sometimes be difficult to determine whether the incriminating fact it establishes has been proved; but rather the indeterminacy of precisely what that fact is.").

Moreover, we think it worth noting that this was not a close case. The government produced copious evidence from a wide range of sources -- from the design of Stratus, to the history of its product development within Acclarent, to how it was promoted to potential customers -- that established an objective intent by Acclarent's management that Stratus be used for delivering Kenalog rather than for its cleared use as a postoperative spacer with

saline. Whatever indeterminacy there might be about how much and what kinds of evidence would be sufficient to prove a new intended use in a close case, appellants cannot rely on that hypothetical indeterminacy to make a vagueness claim here. Cf. McCoy v. Town of Pittsfield, 59 F.4th 497, 509 (1st Cir. 2023) ("[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.'" (Quoting Holder v. Humanitarian L. Project, 561 U.S. 1, 18-19 (2010))).

ii. Inconsistent Agency and Judicial Interpretations

The Supreme Court recognized in Johnson that one powerful indication that a law is unconstitutionally vague is when the law has "proved nearly impossible to apply consistently," engendering "pervasive disagreement" among courts about even "the nature of the inquiry [a court applying the law] is supposed to conduct and the kinds of factors [the court] is supposed to consider." 576 U.S. at 601 (internal quotation marks omitted). We have similarly suggested that where an agency "issues contradictory or misleading public interpretations" of its own regulation, "there may be sufficient confusion for a regulated party to justifiably claim a deprivation of fair notice." Lachman, 387 F.3d at 57.

Appellants raise an inconsistent interpretation argument along these lines by alleging that both the FDA and the courts

have shifted in their interpretation of the FDCA, demonstrating that the term "intended use" is unconstitutionally vague because it has proven subject to varying interpretations. On appellants' telling, the courts and the FDA have at times embraced the narrow view that a medical product's "intended use," is revealed only by promotional statements. At other times, however, they have endorsed the more expansive view that evidence of a product's intended use can come from any relevant source, including not just promotional speech but internal communications, product design, and other conduct.

Appellants suggest that perhaps Caronia is to blame for this shift. To be sure, as we have already observed, Caronia was a significant opinion, articulating a limit on the government's use of off-label promotional speech as the basis of a conviction under the FDCA. It is reasonable to think that the government, as well as courts, may have grown more cautious about using promotional speech alone as the basis of a conviction following Caronia. However, that caution does not mean that Caronia fundamentally altered the way the government or courts construe the applicable law and regulations, opening a door to using non-promotional statements and other conduct as evidence of intended use that was previously (in appellants' telling) closed.

Upon our examination of judicial and agency precedent, we are unpersuaded that there has been such a sea change in the

interpretation of the FDCA that appellants were deprived of fair notice of what the law prohibited. We begin with the caselaw.

Appellants misread the precedent in claiming that courts have exhibited pervasive disagreement about how to understand the determinants of "intended use." Neither of the cases appellants cite exemplify, as they suggest, courts narrowing permissible evidence of intended use to external manufacturer claims only. See Brown & Williamson, 153 F.3d 155; Am. Health Prods. Co. v. Hayes, 574 F. Supp. 1498, 1505 (S.D.N.Y. 1983), aff'd per curiam, 744 F.2d 912 (2d Cir. 1984).

As we explained with regard to Fabian's instructional challenge, the Brown & Williamson court observed that courts typically do not determine intended use without considering manufacturers' external claims, but it did not endorse the distinct notion that only such claims may be considered as evidence of intended use. See 155 F.3d at 163. The court in American Health Products Co. v. Hayes likewise endorsed the unremarkable proposition that "marketing representations" are important in determining intended use but did not say that they alone may be considered. See 574 F. Supp. at 1505.

In fact, as noted above, multiple federal courts of appeal, in decisions stretching back decades, have taken the position that finders of fact may determine "intended use" by considering evidence from a broad range of sources, including

evidence other than promotional claims and other externally directed manufacturer claims. See, e.g., V.E. Irons, 244 F.2d at 38; Allergan, 738 F.3d at 1357; Article of Device, 731 F.2d at 1257; Action on Smoking, 655 F.2d at 239; Article of 216 Cartoned Bottles, 409 F.2d at 739.

As for appellants' suggestion that the FDA has previously interpreted the determinants of "intended use" as encompassing only external promotional claims, the main example they cite comes from a 2002 letter from Daniel E. Troy ("Troy letter"), then Chief Counsel of the FDA. The letter contained Troy's response to requests for information from Applied Digital Systems, see 21 U.S.C. § 360c(g), regarding whether a device the company planned to market was a "medical device" under the FDCA because it was "intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease," see 21 U.S.C. § 321(h)(1)(B). In analyzing two intended uses that the company proposed for the device, Troy stated that "[i]t is well settled that intended use is determined with reference to marketing claims."

The Troy letter does not show that the FDA previously embraced the narrow interpretation of "intended use." First, the Troy letter does not say that external promotional claims are the exclusive source of permissible evidence. As with the caselaw discussed above, a statement that marketing claims are essential

in determining intended use does not foreclose reliance on other factors.[23] Second, per regulation, the views expressed in the Troy letter cannot be attributed to the agency itself, but only to an FDA employee. The letter did not offer an advisory opinion under 21 C.F.R. § 10.85, and it was therefore an "informal communication" that "[did] not necessarily represent the formal position of FDA, and [did] not bind or otherwise obligate or commit the agency to the views expressed." Id. at § 10.85(k). More fundamentally, the fact that the Troy letter was an informal communication to a private regulated entity means that the principle we articulated in Lachman, discussed above, does not apply here. As we emphasized there, "non-public statements" by agency employees do not "create the kind of confusion that supports a finding of a due process violation." 387 F.3d at 58.

[23] The other FDA guidance documents that appellants point to as examples of the FDA adopting the narrow interpretation of the determinants of "intended use" are inapposite for the same reason. Thus, while one guidance document explained that the "FDA has consistently prohibited the promotion of . . . unapproved uses of approved products," nowhere does the document suggest that such promotional claims are the sole permissible evidence of intended use. See Final Guidance on Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64074, 64081 (Dec. 3, 1997). Similarly, while another guidance document mentioned product labeling and information about the product disseminated by manufacturers among the "materials [that] can create new intended uses," the document does not state that these two types of materials are the only permissible determinants of intended use. See Citizen Petition Regarding the FDA's Policy on Promotion of Unapproved Uses of Approved Drugs & Devices, 59 Fed. Reg. 59820, 59821 (Nov. 18, 1994).

2. Fair Warning Claim

Facteau presses an additional due process argument along similar lines. He suggests that in the wake of Caronia, the government has undertaken an interpretive pivot in its enforcement of the FDCA, expanding its definition of intended use to account for the fact that post-Caronia it may be more difficult to carry a conviction based on promotional statements alone. Since appellants' conduct occurred before Caronia but their prosecution came after that decision, Facteau argues that he was convicted by retroactive application of a novel and more expansive interpretation of the relevant FDCA provisions and their accompanying regulations and thus lacked "fair warning" of what the law requires.

A defendant may not be convicted under a penal law that, "either standing alone or as construed," did not make it "reasonably clear at the relevant time that the defendant's conduct was criminal." United States v. Lanier, 520 U.S. 259, 267 (1997). Thus, a defendant has been deprived of "the right of fair warning" when he is convicted under a novel judicial construction of a statute or other law that works "an unforeseeable and retroactive judicial expansion" of the law's scope. Bouie v. City of Columbia, 378 U.S. 347, 352 (1964); see also Lanier, 520 U.S. at 266 ("[D]ue process bars courts from applying a novel construction of a criminal statute to conduct that neither the statute nor any prior

judicial decision has fairly disclosed to be within its scope."). Likewise, where an agency expands its interpretation of a statute or regulation to cover conduct not previously covered, it may not penalize a regulated party for engaging in the newly covered conduct prior to that change in interpretation. See Fox Television Stations, 567 U.S. at 254-58; cf. United States v. Anzalone, 766 F.2d 676, 681-82 (1st Cir. 1985) (concluding that defendant's conviction violated due process because he lacked fair notice of a newly expanded interpretation of the Currency Transaction Reporting Act).

Facteau cannot avail himself of this doctrine. As indicated in our earlier discussion of appellants' vagueness claim, neither the FDA nor the courts, prior to Caronia, espoused an interpretive approach that limited the determinants of intended use to manufacturers' external claims, and thus their interpretation of the law has not broadened following that decision in the way Facteau claims. Beyond those discussed above in connection with appellants' vagueness claim, Facteau cites four cases as examples of decisions where courts have adopted a narrow interpretation of the determinants of "intended use." None of these cases, however, suggests that a product's intended use must be determined exclusively by reference to external promotional claims. Moreover, we find it telling that though Facteau cites all of these cases as examples of the supposed pre-Caronia rule,

some were decided after that case, refuting the suggestion that Caronia spurred a change in how the law is interpreted. Rather, the authority consistently shows, before Caronia and since, that relevant evidence of intended use can come from many sources.

As we have explained, the Eighth Circuit did not hold in Articles of Drug, 50 F.3d 497, that the intended use of a medical product may be determined only by reference to promotional materials. Indeed, the court expressly affirmed that the seller's intended use for a product "may be derived from any relevant source." Id. at 500. Similarly, in United States v. US Stem Cell Clinic, LLC, 998 F.3d 1302, 1311 (11th Cir. 2021), the court suggested that the government must produce marketing materials that support its allegations of a drug's intended use but nowhere stated that only marketing materials are permissible. Likewise, the district court's statement in U.S. ex rel. Modglin v. DJO Global Inc. that a device manufacturer "can only be liable for violating the FDCA if it markets or promotes the device for [an off-label use]," does not limit the range of evidence to such statements. 48 F. Supp. 3d 1362, 1371 (C.D. Cal. 2014) (citing Carson v. Depuy Spine, Inc., 365 F. App'x 812, 815 (9th Cir. 2010)). Whether we agree with these latter two cases that the government must produce evidence of promotional speech to establish a product's intended use is not at issue in this appeal. For the purposes of this case, it is sufficient that we have found

no authority indicating that only promotional statements are relevant to intended use.[24]

We thus discern no interpretive pivot following Caronia. Accordingly, the interpretation of the determinants of "intended use" under which Facteau was prosecuted was not a novel and more expansive interpretation of which he lacked fair warning.

Facteau's fair warning claim fails for a further reason. As the Seventh Circuit has explained, the "uncertainty that is inevitable in legal standards . . . often is offset by [actual] notice, so that people need not guess what is required of them." United States v. Caputo, 517 F.3d 935, 941 (7th Cir. 2008). Hence, where an agency has "alerted [regulated parties] to its view of their legal obligations," and the regulated parties nonetheless choose "to go their own way," they are thereby "[taking] a risk and [cannot] then say 'we didn't know' or 'the regulation left us scratching our heads.'" Id. Here, Acclarent received actual notice. In May 2007, in response to Acclarent's request to add to Stratus's labeling an indication for the delivery of diagnostic and therapeutic substances to the sinuses, the FDA notified Acclarent that the proposed change appeared to be a change in

[24] Facteau's fourth case, Association of American Physicians & Surgeons, Inc. v. FDA, is irrelevant as it did not concern intended use at all. See 226 F. Supp. 2d 204, 216-18 (D.D.C. 2002) (explaining that the question of intended use was not at issue and that the case concerned "a different section of the FDCA entirely").

intended use requiring Acclarent to "submit a new 510(k) and receive Food and Drug Administration clearance prior to marketing [Stratus] with [the proposed] changes."[25] Having been notified of the government's view, Facteau's complaint of unfair surprise at being prosecuted for marketing Stratus to deliver Kenalog despite Acclarent's failure to obtain such approval rings hollow.

D. Fabian's Remaining Arguments

Finally, we turn to several issues that Fabian raises separately: that the evidence is insufficient in the absence of promotional statements specifically pertaining to the ten Stratus shipments underlying the convictions; that Fabian's conviction is improper absent any evidence that he personally participated in submitting Stratus's § 510(k) filings, which he characterizes as the actus reus of the crime; and that his $500,000 fine is excessive under the Eighth Amendment.

1. Sufficiency of the Evidence Arguments

Fabian makes two arguments to challenge the sufficiency of the evidence. Although the government argues that Fabian failed

[25] Facteau argues that because the May 2007 letter indicated that Stratus must receive § 510(k) clearance for use with Kenalog prior to its "marketing" for that use, it did not provide actual notice that Acclarent could not commercially distribute Stratus with that intended use as opposed to making promotional statements about that intended use. We do not agree. In context, "marketing" was a reference to placing Stratus on the market, not to promoting Stratus. In any event, Acclarent did not receive additional clearance before its sales representatives began promoting Stratus for use with Kenalog.

to preserve one of them -- the inadequacy of the evidence on the crime's actus reus -- we disagree and, accordingly, apply de novo review to both sufficiency claims.[26] See United States v. Cadden, 965 F.3d 1, 10 (1st Cir. 2020). Our task is therefore to "assess the record evidence 'in the light most favorable to the prosecution' and affirm so long as the 'body of proof, as a whole, has sufficient bite to ground a reasoned conclusion that the government proved each of the elements of the charged crime beyond a reasonable doubt.'" Id. at 10 (quoting United States v. Lara, 181 F.3d 183, 200 (1st Cir. 1999)).

i. Evidence of Intended Use Accompanying Each Shipment

Fabian argues that the government needed to adduce evidence -- in the form of commercial expression -- accompanying each of the ten shipments of Stratus underlying the conviction to

[26] The government asserts that Fabian is not entitled to de novo review of the actus reus claim because he did not specifically brief that claim in the district court. We have held, however, that a Rule 29 motion raising a "general challenge to the adequacy of the evidence preserves for de novo review 'the full range of challenges, whether stated or unstated.'" United States v. Marston, 694 F.3d 131, 134 (1st Cir. 2012). Only if a defendant "give[s] specific grounds for a Rule 29 motion" is there a waiver of "all grounds not specified." Id. Although appellants' Rule 29(c) motion specifically challenged only the evidence pertaining to the ten shipments of Stratus, their Rule 29(a) motion "assert[ed] a general challenge to the sufficiency of the Government's evidence on all counts." We consider this statement adequate to generally preserve the issue of sufficiency of the evidence. See id. at 135 (urging "in case of doubt to treat an ambiguous motion . . . as 'general'" to avoid "penaliz[ing] the giving of examples" or "creat[ing] a trap for the unwary defense lawyer").

establish the intended use of that particular shipment. The government having failed to carry this burden, Fabian argues, his conviction stands on insufficient evidence. We disagree.

To start, Fabian's argument as presented seems to depend upon his theory that only outward promotional speech is probative of a product's intended use. Accordingly, Fabian asserts that the government needed to, but did not, put forward evidence of statements accompanying each shipment of Stratus promoting that shipment for use with Kenalog rather than saline. As we have explained, Fabian is incorrect that only promotional statements can establish a product's intended use, and his argument thus falters out of the gate.

In any case, we do not agree with Fabian's underlying premise that the government must always put forward evidence establishing the intended use of each individual shipment, even when the evidence shows that the whole point of the enterprise was to market an adulterated and/or misbranded device. Fabian seems to suggest that it is the act of shipping, itself, that renders a device adulterated or misbranded, such that the circumstances of each shipment are essential to the status of the device. But that is not so. We have long said that § 331(a) "prohibit[s] the introduction into interstate commerce of [products] which at the time of introduction" are adulterated or misbranded. Penobscot Poultry Co. v. United States, 244 F.2d 94, 97 (1st Cir. 1957).

In other words, a device must in its "present state" at the time of shipping be adulterated or misbranded, but the circumstances of the shipment need not render it so. Id.

To be sure, the immediate circumstances accompanying a device's shipment may provide evidence of its intended use, but so may all sorts of evidence from before (or after) the shipment that establish the essential fact under § 331(a): that the device was misbranded or adulterated when shipped. Here, the record evidence reflects a scheme that from the beginning was aimed at marketing Stratus to deliver Kenalog rather than saline, including evidence that Stratus did not even work to deliver saline, was specifically designed with Kenalog in mind, and was promoted with a sales strategy devised to get physicians to associate Stratus with Kenalog and consider using it for drug delivery. As the Acclarent executive in charge of sales, Fabian oversaw much of this activity. A reasonable juror could examine this evidence and find that any Stratus shipped by Acclarent in the midst of that scheme had an intended use of delivering Kenalog.

In arguing that the evidence needed to establish the intended use of each shipment, Fabian largely relies on Kordel v. United States, 335 U.S. 345 (1948), and, once again, on the Eighth Circuit's decision in Articles of Drug, 50 F.3d 497. Neither case lends Fabian the support he claims. Kordel does not, as Fabian suggests, stand for the broad principle that any conviction for

violating the FDCA by marketing an unapproved product requires evidence (of promotional statements or otherwise) accompanying that specific shipment to establish the intended use of the shipped product. The defendant in Kordel was convicted of misbranding a drug by marketing it with an inadequate or false label. Whether promotional statements had to directly accompany individual shipments of a product to establish liability was a relevant issue in that case because the statute defined a drug label to include "written, printed, or graphic matter . . . accompanying such article." Kordel, 335 U.S. at 347 (citing 21 U.S.C. § 201(m)) (emphasis added). Here, by contrast, Fabian is not accused of mislabeling a drug product, and thus the scope of the statutory requirement that statements or other materials "accompany" a product to be considered part of the product's labeling is irrelevant. The statutory and regulatory scheme at hand speaks of no similar requirement that materials or other evidence must "accompany" the individual product unit to shed light on its intended use.[27]

Nor does Articles of Drug lend any persuasive force to Fabian's argument. The court did express that "[p]romotional

[27] Our decision in Nature Food Centres, Inc. v. United States, 310 F.2d 67 (1st Cir. 1962), is similarly inapposite. That case, too, discussed the requirement that materials "accompany" shipped products in the specific context of labeling, drawing that requirement directly from the statutory and regulatory scheme. Id. at 70-71.

materials are relevant to intent so long as they are currently being distributed with the product . . . ." Articles of Drug, 50 F.3d at 500. But nothing in the court's analysis suggests that the caveat that promotional material be "current" -- which also harkened to the requirement that drug labeling "accompany" the product, see 21 U.S.C. § 201(m) -- should extend to other forms of evidence. To the contrary, the court expressly recognized that "intended application for a product may be derived from any relevant source." Articles of Drug, 50 F.3d at 500 (emphasis added). Indeed, it even held that past promotional efforts not tied to a particular shipment can be probative of a product's intended use in appropriate cases. Id. As we have discussed, the evidence in this case may not be contemporaneous with individual shipments, but it provided ample reason for jurors to conclude that the intended use of Stratus, generally, was to deliver Kenalog, and thus that each shipment of Stratus underlying Fabian's conviction shared that intended use.

ii. Evidence of Actus Reus

In his second sufficiency challenge, Fabian argues that the government failed to produce evidence that would allow a rational jury to conclude that he participated in the actus reus of the crime, which, in his telling, was Acclarent's § 510(k) filings with the FDA. Fabian asserts that, because no record evidence showed that he participated in preparing regulatory

filings for the company, he could not have committed what he argues is the criminal act underlying the conviction. Nor, as vice president of sales, could he have been considered a responsible corporate agent for that act. See United States v. Dotterweich, 320 U.S. 277, 284 (1943); United States v. Park, 421 U.S. 658, 673-74 (1975). The government counters that the true actus reus of violating § 331(a) is "caus[ing] the introduction of an adulterated or misbranded article into interstate commerce." The government insists that a rational jury could conclude from the evidence that Fabian, the company's chief salesman, participated in introducing Stratus -- which the jury otherwise concluded was a misbranded and adulterated device -- into interstate commerce.

We agree with the government's assessment, starting with how to properly characterize the actus reus of the crime. Section 331(a), upon which Fabian's conviction stands, 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). Plainly enough, the prohibited act under the statute is causing a misbranded or adulterated device to be introduced into interstate commerce. To be sure, the fact that the device is misbranded or adulterated (and that the article is a device to begin with) is a separate element of the offense, which the government must prove to carry a conviction. But it does not

follow -- and nothing in § 331(a) suggests -- that the government must prove that the defendant caused it to be misbranded.

Our recent analysis in United States v. Stepanets, 989 F.3d 88, 95 (1st Cir. 2021), is instructive. As relevant here, Stepanets concerned an appeal from a conviction under 21 U.S.C. § 331(a) for delivering a misbranded drug into interstate commerce. The government's theory on misbranding turned on 21 U.S.C. § 353(b)(1), which provides that "the act of dispensing a drug" absent a proper prescription "shall be deemed to be an act which results in the drug being misbranded while held for sale." The defendant urged us to overturn the conviction on the ground that the record contained no evidence that she, personally, had dispensed the drug improperly, thereby misbranding it. While we ultimately found it unnecessary to reach that issue, we expressed doubt that the statutory scheme required such a showing. See Stepanets, 989 F.3d at 95. After all, the prohibited act under the statute is "causing . . . [t]he introduction or delivery for introduction into interstate commerce of any" such drug. 21 U.S.C. § 331(a). Section 353(b)(1) explained why the drug was misbranded, but, as we pointed out, nothing in § 331, under which Stepanets was charged, required the government to prove that she had personally caused the drug to become misbranded, so long as she caused the misbranded drug to enter interstate commerce. Stepanets, 989 F.3d at 95.

Likewise, here, Fabian was convicted under § 331(a) for causing an adulterated or misbranded device to be introduced into interstate commerce. The government's theory on adulteration or misbranding turns on different FDCA provisions from those at issue in Stepanets, but our analysis there is equally applicable here. That is, the jury in this case needed to determine that the device was adulterated or misbranded (or both), but it did not need to conclude that Fabian caused the adulteration or misbranding. As we observed in Stepanets, § 331(a) speaks of no such requirement, but only of "causing . . . [t]he introduction or delivery for introduction into interstate commerce of any . . . device . . . that is adulterated or misbranded."

Accordingly, we reject Fabian's assertion that the government needed to prove that he participated in the Stratus § 510(k) filings.[28] Evidence that Fabian caused the device to

[28] Fabian claims that the district court's order denying appellants' motion for acquittal characterized the actus reus as he does on appeal. That claim is mistaken. In its order, the court stated that the actus reus for marketing a misbranded device was "Defendants' failure to submit a premarket notification for the intended use" of the drug. Facteau, 2020 WL 5517573, at *14 (emphasis added). In other words, the district court described the actus reus as marketing a device that lacked the proper regulatory clearance, which rendered it misbranded and adulterated under the FDCA. See 21 U.S.C.A. § 352(o). For both the adulteration and misbranding counts, the court's instructions on the second element of the crimes further made clear the actus reus by appellants that the jury needed to find: "caus[ing]" an adulterated or misbranded device "to be introduced into interstate commerce."

enter into interstate commerce was sufficient -- assuming, as the jury found here, that the device was indeed adulterated or misbranded.

Fabian does not specifically challenge the sufficiency of the government's evidence to establish that he caused Stratus to enter interstate commerce, nor could he. As we have discussed, the record is replete with evidence showing that Fabian, as Acclarent's vice president of sales, had a hand in marketing Stratus and thereby caused it to enter interstate commerce. Moreover, even in the absence of evidence specifically tying Fabian to the strategy of marketing Stratus to deliver Kenalog, the jury's verdict would stand under Dotterweich, 320 U.S. 277, and Park, 421 U.S. 658. These cases -- both concerning violations of § 331 of the FDCA -- stand for the proposition that the statute is violated by anyone who has "a responsible share in the furtherance of the transaction which the statute outlaws, namely, to put into the stream of interstate commerce adulterated or misbranded drugs." Dotterweich, 320 U.S. at 284. Thus, the government's evidence is sufficient to sustain a conviction under § 331 of an individual who "had, by reason of his position in the corporation, responsibility and authority either to prevent in the first instance, or promptly to correct, the violation complained of, and [who] failed to do so," even absent direct evidence tying the defendant to the act. Park, 421 U.S. at 673-74. Charged with

spearheading Acclarent's sales and marketing strategy for Stratus, Fabian was well-situated to prevent or correct the marketing of adulterated and misbranded Stratus, and it was reasonable for the jury to find him culpable for failing to do so.

2. Excessive Fines Clause

Fabian challenges the $500,000 fine the district court imposed on him. He asserts that this fine, which is 2.5 times the recommended guidelines amount but well within the statutory maximum, is excessive in violation of the Eighth Amendment. The government counters that Fabian has waived any such argument, and, regardless, his challenge fails the test laid out in United States v. Bajakajian, 524 U.S. 321 (1998), and our cases applying it.

The government's argument for waiver is not without merit. Not only did Fabian fail to lodge an Eighth Amendment objection to the fine at sentencing, but he also acknowledged that the court could depart from the guidelines up to the statutory maximum. Nonetheless, we choose to deem the Eighth Amendment claim forfeited rather than waived and, as in similar cases, we will review the district court's judgment for plain error. See, e.g., United States v. Sepúlveda-Hernández, 752 F.3d 22, 36 (1st Cir. 2014); United States v. Aguasvivas-Castillo, 668 F.3d 7, 16 (1st Cir. 2012); United States v. Beras, 183 F.3d 22, 28 (1st Cir. 1999). See also Fed. R. Crim. P. 52(b) ("A plain error that affects substantial rights may be considered even though it was

not brought to the court's attention."). Fabian therefore "must show '(1) that an error occurred (2) which was clear or obvious and which not only (3) affected [his] substantial rights, but also (4) seriously impaired the fairness, integrity, or public reputation of judicial proceedings.'" Nieves-Meléndez, 58 F.4th at 579 (quoting Merced-García, 24 F.4th at 79-80).[29]

Fabian has not made that showing. For a fine to be excessive under the Eighth Amendment, it must be "grossly disproportional to the gravity of the defendant's offense." Bajakajian, 524 U.S. at 337. We have distilled from the Supreme Court's guidance three factors that courts must consider: "(1) whether the defendant falls into the class of persons at whom the criminal statute was principally directed; (2) other penalties authorized by the legislature (or the Sentencing Commission); and (3) the harm caused by the defendant." United States v. Heldeman, 402 F.3d 220, 223 (1st Cir. 2005) (citing Bajakajian, 524 U.S. at

[29] The government further contends that Fabian waived plain error review by failing to apply this four-factor test in his opening brief. While that is true, his arguments make apparent his theory of the district court's plain error, and he did squarely address the plain error factors in his reply brief. See United States v. Serrano-Delgado, 29 F.4th 16, 27 (1st Cir. 2022) (citing United States v. Pabon, 819 F.3d 26, 33–34 (1st Cir. 2016)) ("[P]lain error review is waived if its four-part test is not argued at least in reply."). Moreover, "'[w]here a defendant's claim would fail even if reviewed for plain error, we have often' simply proceeded to the merits." Grullon, 996 F.3d at 32 (alteration in original) (quoting United States v. Brake, 904 F.3d 97, 99 (1st Cir. 2018)). As we explain, Fabian's Eighth Amendment claim fails under plain error review.

337-40).[30] Nothing from this guidance suggests that the fine the district court imposed was in error.

First, as an executive of a medical device company -- and one specifically tasked with marketing its products -- Fabian falls squarely within "the class of persons at whom [§ 331(a)] [is] principally directed." Id.[31] Second, comparison to the "other penalties authorized by the legislature (or the Sentencing Commission)" shows that the fine the district court imposed is not excessive. Id. Notably, Fabian's fine is only half of the maximum fine authorized by the statute. See 18 U.S.C. § 3571(b)(5). Indeed, Facteau, Fabian's co-defendant, was

[30] Bajakajian and Heldeman both concerned forfeitures rather than literal fines like the one at issue in this case. However, both cases considered those forfeitures to be fines within the meaning of the Excessive Fines Clause. See Bajakajian, 524 U.S. at 328 ("Forfeitures -- payments in kind -- are thus 'fines' if they constitute punishment for an offense."). Hence, the principles announced in Bajakajian and distilled in Heldeman are equally relevant when considering actual fines rather than forfeitures.

[31] Fabian suggests, without citation, that the first Heldeman factor is relevant only to cases involving forfeitures and therefore does not apply to the fine here. We do not agree. In Bajakajian, the Supreme Court considered whether the defendant fell within the class of people at whom the statute was directed not because the penalty at issue was a forfeiture but to determine if the penalty corresponded to the defendant's conduct. In that case, the statute was "principally designed" to stop the activity of "money launderer[s], drug trafficker[s], [and] tax evader[s]," but the defendant was none of these things -- he was carrying the forfeited cash to pay off a lawful debt. Bajakajian, 524 U.S. at 338. By contrast, § 331(a) is principally directed at those, like Fabian, who sell medical devices (among other products covered by the FDCA).

convicted of the same ten counts as Fabian but received the statutory maximum fine of $1 million. Where a fine falls below the statutory maximum, we have suggested that "a defendant who purposes to challenge its constitutionality faces an especially steep uphill climb." Sepúlveda-Hernández, 752 F.3d at 37.

Fabian emphasizes that his fine is more than twice the maximum amount stated in the sentencing guidelines, which at the time of Fabian's offense was $200,000. See U.S.S.G. § 5E1.2(c)(3) (2014) (maximum fine of $20,000 per count for level 10 offenses). True, we have inferred from Bajakajian that "the maximum penalties provided under the Guidelines should be given greater weight than the statute because the Guidelines take into consideration the culpability of the individual defendant." Beras, 183 F.3d at 29 n.5 (citing Bajakajian, 524 U.S. at 339 n.14). But that caution does not mean that any fine exceeding the Guidelines, yet within the statutory maximum, becomes per se unconstitutional. In United States v. Carpenter, for example, we observed that the Guidelines were calibrated to the "gain or loss resulting from the offense," sanctioning an upward departure when necessary to achieve that aim. 941 F.3d 1, 11 n.8 (1st Cir. 2019) (quoting U.S.S.G. § 5E1.2 cmt. n.4). There, we ultimately upheld a forfeiture of $14 million, which dwarfed the maximum guideline sentence of $100,000. Here, the district court reasoned that Fabian's crime warranted a hefty financial penalty because "[t]his was a crime about money"

and "in the corporate environment in which we live," the "best way" to "accomplish general deterrence" is by "financial penalty." The district court thus justified its decision to exceed the Guidelines with a thoughtful explanation that reveals no error.

Finally, while the record does not show injury to others or financial harm, damage to the government's regulatory interests is also an important consideration. See, e.g., United States v. Jose, 499 F.3d 105, 112 (1st Cir. 2007) (choosing to "adhere to Congress's view that defendant's violation of the bulk cash smuggling statute constitutes a significant harm," without noting any direct harm to individuals resulting from his actions); Aguasvivas-Castillo, 668 F.3d at 17 (stating that harm from defendant's food stamp fraud included "introduc[ing] waste into the program," undermining efforts to "reduce opportunities for fraud," and subverting Puerto Rico's judgment about how to administer its food stamp program).

Here, the district court noted the regulatory harm of Fabian's conduct, remarking:

> I feel [it] is critically important to protect . . . the integrity of the regulatory process. . . . I think that the FDA is important. I think that they try very hard to do what is a very difficult job, and it is important to maintain the integrity of this process for them.
>
> And again as I noted [in Facteau's sentencing hearing], particularly in the time of COVID, it's become just starkly clear how important

> it is that the public have confidence in what the FDA does.

The district court's conclusion that these harms to the government's regulatory prerogatives warranted serious punishment, even in the absence of recorded harm to any individual, is well-founded. After all, the FDCA reflects Congress's longstanding view that marketing unadulterated or misbranded medical devices is a serious offense, the violation of which endangers public health and harms the government's interests in ensuring public confidence in the market for products overseen by the FDA.[32]

Because we conclude that the district court's sentence was not in error, much less plain error, we find that Fabian's fine of $500,000 passes muster under the Eighth Amendment.

III.

To briefly recap our holdings, we conclude that appellants' convictions did not violate the First Amendment or

[32] See, e.g., POM Wonderful LLC v. Coca-Cola Co., 573 U.S. 102, 108 (2014) ("The FDCA statutory regime is designed primarily to protect the health and safety of the public at large."); Brown & Williamson Tobacco Corp., 529 U.S. at 133 ("[O]ne of the Act's core objectives is to ensure that any product regulated by the FDA is 'safe' and 'effective' for its intended use. . . . This essential purpose pervades the FDCA."); In re Zofran (Ondansetron) Prod. Liab. Litig., 57 F.4th 327, 330 (1st Cir. 2023) ("Congress enacted the Food, Drug, and Cosmetic Act (FDCA) in 1938 'to bolster consumer protection against harmful products.'" (quoting Wyeth v. Levine, 555 U.S. 555, 574 (2009))). See also 21 U.S.C. § 393(b)(2) (defining the FDA's mission as "protect[ing] the public health by ensuring that . . . there is reasonable assurance of the safety and effectiveness of devices intended for human use").

constitutional due process, that the district court's instruction to the jury that it may consider evidence of intended use from any relevant source was proper, that Fabian's conviction was supported by sufficient evidence, and that Fabian's fine did not violate the Eighth Amendment. We therefore affirm appellants' convictions and Fabian's fine.

So ordered.