UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

UNITED STATES OF AMERICA	)	
v.	)	
WILLIAM FACTEAU, PATRICK FABIAN	)	Criminal No. 15-10076-ADB
Defendants.	)	

GOVERNMENT'S OPPOSITION TO
DEFENDANTS' MOTION FOR JUDGMENT OF ACQUITTAL OR,
ALTERNATIVELY, A NEW TRIAL

TABLE OF CONTENTS

Introduction.....1

I. The Legal Standards Applicable to Rule 29 Motions.....2

II. Defendants' Convictions Do Not Violate the First Amendment 3

A. The Defendants Were Convicted of Distribution of Adulterated and Misbranded Devices – Not Speech Crimes.....3

B. Truthful Speech May Be Evidence of Any Element of a Crime.....6

C. The Verdict Does Not Establish That All Speech Was Truthful and Non-Misleading and Evidence Established It Was Not.....8

D. The FDCA's Misbranding and Adulteration Provisions as Applied in this Prosecution of Defendants Survive First Amendment Scrutiny.....12

1. The Government Has a Substantial Interest in Requiring Review of Medical Products for Their Intended Uses *Before* They Are Marked and Distributed to Patients for Those Uses.....14

2. Application of the Adulteration and Misbranding Provisions of the FDCA to this Case Is Not More Extensive than Necessary 18

III. Courts Have Held that the FDCA, Its Misdemeanor Provisions and Intended Use Concept Do Not Violate Due Process.....22

A. The Controlling Authority Holds that the FDCA and Its Intended Use Provisions Are Not Unconstitutionally Vague 22

B. Intended Use Concept Is Fundamental to the Entire FDCA Regulatory Scheme to Protect Patients from Unsafe Medical Products 25

C. This Court Correctly Rejected Claims That Only External Marketing Statements Can Serve As Evidence of Intended Use 27

D. Evidence of "Probing Questions" Was Appropriate.....33

E. Lack of Scienter Requirement Does Not Make an Otherwise Unambiguous Statute Unconstitutionally Vague 34

IV. There Was More Than Sufficient Evidence For Jury to Find Ten Shipments Adulterated And/Or Misbranded 39

V. The Convictions for Adulteration and Misbranding Are Not Mutually Exclusive.....45

VI. Defendants Are Not Entitled to A New Trial 46

A. Evidence About the Stratus' Safety Was Not Improper or Unduly Inflammatory.....47

B. Defendants Are Not Entitled to a New Trial Simply Because the Government Did Not Immunize Debra Cogan 49

VII. Inconsistent Witness Testimony Does Not Show Misconduct 49

A. Questions About Knowledge of On-Label Use Are Entirely Proper.....51

B. Potentially Inconsistent Memories of Convery and Steffen Do Not Establish Misconduct.....52

C. Asking Whether A Defendant Was Present Is Not Misconduct 53

D. Asking About How Acclarent Handled Trade Shows Is Not Improper 53

Conclusion 54

INTRODUCTION

A jury convicted both William Facteau and Patrick Fabian of ten counts of introducing medical devices into interstate commerce without the required FDA approval and notice. The evidence was overwhelming that this device was never intended or marketed for its sole FDA-cleared use as a post-operative spacer to be filled with saline. In fact, the evidence established that the Stratus did not work for that use.

Defendants and their Amici's constitutional challenges are without merit. They are contrary controlling precedent. Moreover, this Court's instructions to the jury simply did not permit the jury to convict by treating truthful, non-misleading speech as the crime – thereby obviating any First Amendment issue.

Nor was there anything incendiary or improper about how the government tried this case. To the contrary, the government was forthright with the jury from opening through closing that there were no deaths, blindness or "anything like that." 2 Trial Tr. 50, 26 Trial Tr. 60.

The Defendants and their Amici seek to use this case to challenge the role of the FDA and it regulatory process, but their challenges fail to address the facts of this case, or acknowledge this Court's repeated and unequivocal instructions to the jury that truthful, non-misleading speech was not the crime here. The evidence at trial established that this is not a case about a company legitimately distributing a medical product for a valid on-label use and seeking to share balanced scientific information or studies. It is a case about distributing medical devices without the demonstration of safety and efficacy that Congress has mandated before such devices are distributed to the nation's patients. The evidence at trial clearly demonstrated that the Defendants committed the crimes of which they were convicted. There is no basis to set aside the jury's verdict.

I. THE LEGAL STANDARDS APPLICABLE TO RULE 29 MOTIONS[1]

Rule 29 permits a Court to enter a judgment of acquittal only if the "evidence is insufficient to sustain a conviction." Fed. R. Crim. P. 29. "If the evidence presented, taken in the light most flattering to the prosecution, together with all reasonable inferences favorable to it, permits a rational jury to find each essential element of the crime charged beyond a reasonable doubt, then the evidence is legally sufficient." United States v. Olbres, 61 F.3d 967, 970 (1st Cir. 1995).[2] In considering a Rule 29 Motion, the court must "'scrutinize the evidence in the light most compatible with the verdict [and] resolve all credibility disputes in the verdict's favor.'" United States v. Merlino, 592 F.3d 22, 29 (1st Cir. 2010) (citations omitted).[3]

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[1] The United States also incorporates by reference its prior filings on the same issues. See Dkt. 224, Gov't Omnibus Opposition to Defendants' Motions to Dismiss at 5-12 (First Amendment); 12-14 (evidence of external marketing claims as to "intended use"); 14-30 (void for vagueness); 30-35 (misdemeanors); see also id. at 70-71 (addendum identifying which pages of Government's brief addresses which argument of Defendants). The United States is also providing an electronic copy of all trial transcripts and government exhibits with a courtesy copy of this opposition.

[2] Defendants rely on a Declaration of Jeffrey Shapiro, an attorney consultant whom they retained as an expert for this case. See Defs.' Br. at 11, 14, 20-22, 48. Defendants chose not to call Mr. Shapiro to testify after the Court limited the scope of his expected testimony. In considering the Rule 29 Motion, the Court must disregard his declaration and the exhibits thereto, which were never admitted into evidence. See United States v. Figueroa-Lugo, 915 F. Supp. 2d 237, 241 (D.P.R. 2013) (noting that courts "assess[] only the admissible evidence at trial in applying the sufficiency standard."), aff'd, 793 F.3d 179 (1st Cir. 2015); see also United States v. Edwards, 488 F.2d 1154, 1161 (5th Cir. 1974) (declining to consider records of defendant's psychiatric history in context of motion for judgment of acquittal where the materials were submitted "outside the record"). See generally United States v. Prigmore, 243 F.3d 1, 18 n.3 (1st Cir. 2001) ("We feel it important to note, however, that expert testimony proffered solely to establish the meaning of a law is presumptively improper.").

[3] Furthermore, as Judge Wolf's analysis in DiMasi demonstrates, a Rule 29 acquittal would be inconsistent with this Court's previous Petruzziello findings. See United States v. DiMasi, 810 F. Supp. 2d 347, 351 (D. Mass 2011), aff'd sub nom. United States v. McDonough, 717 F.3d 143 (1st Cir. 2013). This Court found by a preponderance of the evidence to establish a

II. DEFENDANTS' CONVICTIONS DO NOT VIOLATE THE FIRST AMENDMENT.

A. The Defendants Were Convicted of Distribution of Adulterated and Misbranded Devices – Not Speech Crimes.

The crimes for which Defendants were convicted were distribution of a medical device that lacked the required FDA approval and premarket notice. Not a single element of either crime was speech. As discussed below, the Court's instructions and the Government's case were clear and repeatedly reminded the jury that the crime was not speech, but distribution of a medical device for a use for which it was not cleared or approved by FDA. The Court's instructions included the following:

> It is not illegal in and of itself for a device manufacturer to provide truthful, not misleading information about an off-label use. The FDCA does not prohibit or criminalize truthful, not misleading off-label promotion. You may not convict a Defendant of a crime 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. . . .
>
> The indictment in this case does not charge any defendant with the crime of promoting a device off-label, because that is not itself a crime. Rather, the FDCA crimes charged are conspiring to introduce, and causing the introduction of, devices into interstate commerce that were adulterated or misbranded. Although you may not convict a Defendant of a crime based solely on truthful, non-misleading statements regarding off-label use, even truthful statements about an off-label use can be considered as evidence. To put it another way, to convict, there must be a criminal act. Truthful, non-misleading speech cannot be a criminal act in and of itself, but it can be evidence and therefore used by you to determine whether the government has proved each element of each offense beyond a reasonable doubt, including the element of intent . . .
>
> Off-label promotional statements can constitute evidence of an intended use, although truthful, non-misleading speech alone cannot be the basis for a criminal

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conspiracy to commit the FDCA violations charged – which the Court instructed the jury required some level of criminal intent, and was subject to a good faith defense. Since the evidence was sufficient to establish such an intentional conspiracy, at least by a preponderance; a reasonable juror could have found the FDCA misdemeanors, which did not require criminal intent and were not subject to the good faith defense, beyond a reasonable doubt.

> conviction. Neither the First Amendment nor any other law, however, protects false or misleading speech.
>
> In addition, it is permissible to respond to unsolicited requests for information about FDA-regulated medical products by providing truthful, balanced, non-misleading, and non-promotional scientific or medical information that is responsive to the specific request, even if responding to the request requires a manufacturer to provide information on unapproved or uncleared indications or conditions of use. Under these circumstances, such responses may not be considered as evidence of a new or different "intended use."

Dkt. 436 at 26-27 (Off-Label Promotion and Intended Use Jury Instructions). The Court's instructions were clear that speech is not the crime and the jury could not convict the Defendants based upon truthful, non-misleading speech alone. Juries are presumed to follow their instructions. See Weeks v. Angelone, 528 U.S. 225, 234 (2000). Thus the jury's verdict could not have rested on truthful, non-misleading speech alone or treating it as the criminal act.

Also, contrary to Defendants' and the Amici's repeated claims, this not the case where, but for the speech, there would have been no crime. Distribution of the Stratus for the intended purpose of drug delivery, without FDA clearance or approval for that use, was a crime independent of any promotional claims. Any truthful, non-misleading promotional speech was evidence of that crime, but not itself the criminal act. Moreover, such speech evidence was cumulative of other evidence showing that Stratus was always intended to serve as a drug delivery device and not to be used for its cleared use. A reasonable juror could have found Defendants guilty based on evidence showing that the Stratus did not work for its cleared use.

The first witness, Dr. Armstrong, observed that the Stratus "did not hold water" for its FDA cleared use in a demonstration at the Acclarent-sponsored Sinus Forum, just as the product

was being launched.[4] The evidence at trial demonstrated that Defendants were told by their own scientific advisors, as well as the engineer who designed the device, that it did not work with saline and was designed to elute the more viscous suspension Kenalog-40.[5] Also, contrary to Defendants' claim, this is not a case where the device merely had a design feature that might one day be used for another intended use. By designing the holes of the device to elute Kenalog specifically, Acclarent designed them ***NOT*** to elute saline slowly – i.e. not to inflate and mechanically hold open a space over the period of implantation as claimed in the product labeling.[6] See United States v. Caputo, 517 F.3d 935, 937, 940-42 (7th Cir. 2008) (upholding conviction where evidence of a major change in intended use included that the defendant

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[4] See 3 Trial Tr. 61-63 (Armstrong: saline "squirted out" of Stratus at Sinus Forum and "did not inflate" and "therefore cannot work as labeled"); GX808 (Armstrong email to Acclarent explaining Stratus "does not hold water as advertised").

[5] See 7 Trial Tr. 167:2-9 (Oakes: SAB members discussing saline "run[ing] out very rapidly because those pore sizes would not have been designed to work effectively with saline"); GX706 at ACC-034-0004111 ("We have conducted R&D testing to determine which fluids would be expected to drip from the device over extended time periods. Our testing demonstrates that most common antibiotics would washout of the device very rapidly."); GX415 (Ketan Muni: "As we are not releasing saline over 14 days, we should take that statement out."); 10 Trial Tr. 25, 28 ((Krinsky: learned in training that holes were "specially sized" for Kenalog; Krinsky: saline ran out "quickly" – in "seconds").

[6] See supra n.5; see also GX457 (2/5/08 Cogan email stating "surprise, surprise" when saline ran out of Stratus implanted and injected with saline); 4 Trial Tr. 154, 208 (Vanderkarr: Stratus micropores designed for Kenalog 40 and "any other substance … would just kind of leak out"; explaining understanding that "saline … would just run out"); 7 Trial Tr. 87, 106 (Steffen: injected saline "came right out" and Stratus "didn't work with saline"); 9 Trial Tr. 59 (Convery: saline eluted from Stratus "quickly ….[l]ess than ten minutes"); 10 Trial Tr. 60-61 (Logan: "micropores were sized to slowly weep out Kenalog 40" and that saline "would run out immediately"); 11 Trial Tr. 83 (Bilsbury: learned in training and heard in Elmore's FESS by Numbers presentation that the pores were designed for Kenalog); see GX1428 at ACC-044-0000739 (Elmore FESS by Numbers presentation explaining that Stratus pores "specifically tailored for the large molecules that is [*sic*] Kenalog 40").

changed the physical properties of the device – made it bigger – so it could be used to sterilize different medical instruments).

Moreover, a reasonable juror might well infer intended use from the lack of any market, claims or promotional materials about the FDA-cleared use.[7] This is not a case, unlike cases relied upon by Defendants and their Amici, where a drug or device with a legitimate market for its approved use was promoted for both its approved use and unapproved uses. In this sense, this case is similar to Caputo, where the Court noted that there was no market for the small Plazlyte machine and the defendant had not tried to sell it for its FDA-cleared use. Caputo, 517 F.3d at 937 ("Caputo understood that Abtox would never be able to sell a single unit of the small Plazlyte for the limited use approved by the FDA. Caputo … did not try."). Likewise here, the lack of claims or a market for the cleared use made it obvious that Stratus was intended as a drug delivery device.

B. Truthful Speech May Be Evidence of Any Element of a Crime.

[7] See 4 Trial Tr. 179 (Vanderkarr: did not believe she could ever sell Stratus for use with saline); 198 (Vanderkarr: was not willing to recommend Stratus for cleared use because she did not see any benefit); 7 Trial Tr. 37 (Vanderkarr: did not think she could sell any Stratus for use with saline); 7 Trial Tr. 106 (Steffen: not possible to sell Stratus for use with saline because it didn't work and the sales representative would "lose credibility"); 166 (Oakes: SAB told Acclarent that there was no therapeutic value to using Stratus with saline); 11 Trial Tr. 35-36 (Ader: would not have sold Stratus if he followed regulatory training on FDA compliance); 15 Trial Tr. 32 (Hwang: no therapeutic value in having a reservoir in the sinus to deliver saline); 18 Trial Tr. 186 (Citardi: Stratus could not function as a spacer because it did not hold volume, so he wa.s not interested in using it for that purpose); 24 Trial Tr. 41 (Catalano: Stratus was "useless" as a mechanical stent); 8 Trial Tr. 130 (Dr. Chong: Stratus would "not be useful as a stent"); 4 Trial Tr. 156 (Vanderkarr: could not recall any pitches or talk tracks provided "to recommend to a physician the use of the device as a spacer with saline"); 9 Trial Tr. 71 (Convery: could not recall any sales force meetings discussing benefits of Status as spacer with saline); 10 Trial Tr. 25-29 (Krinsky: never trained on any benefit of Stratus as spacer with saline); 10 Trial Tr. 64-65 (Logan: no one trained her on benefits of Stratus with saline or how to promote it for that use); 11 Trial Tr. 24-29 (Ader: never trained on benefit of Stratus with saline; never received sales tools, literature or videos relaying benefits of Stratus as spacer with saline).

As the Court instructed the jury, truthful, non-misleading speech can be evidence of any element of a crime. "The First Amendment . . . does not prohibit the evidentiary use of speech to establish the elements of a crime or to prove motive or intent. Evidence of a defendant's previous declarations or statements is commonly admitted in criminal trials." Wisconsin v. Mitchell, 508 U.S. 476, 489 (1993) (holding sentencing enhancement for defendant's targeting victim based on race did violate First Amendment); Wine & Spirits Retailers v. Rhode Island, 418 F.3d 36, 50-51 (1st Cir. 2005) ("[T]he State does not lose its power to regulate commercial activity deemed harmful to the public whenever speech is a component of that activity.").[8]

Courts have applied this precedent to reject First Amendment challenges to the Federal Food, Drug, and Cosmetic Act (FDCA), holding that "th[e] use of speech to infer intent, which in turn renders an otherwise permissible act unlawful, is constitutionally valid" and hence "it is constitutionally permissible for the FDA to use speech [by the manufacturer] . . . to infer intent for purposes of determining that [the manufacturer's] proposed sale . . . would constitute the forbidden sale of an unapproved drug." Whitaker v. Thompson, 353 F.3d 947, 953 (D.C. Cir. 2004); United States v. Lebeau, 2016 WL 3619838, at *3 (7th Cir. 2016) (rejecting First Amendment challenge to misdemeanor unapproved new drug conviction where promotional claims were introduced as evidence, noting "[t]he prosecutor used LeBeau's statements only to show how he intended consumers to use his product, and thus, whether the product is a drug"); United States v. Pfizer, 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

[8] See also Flytenow, Inc. v. FAA, 808 F.3d 882, 894 (D.C. Cir. 2015) (upholding "speech (postings on Flytenow.com) as evidence that pilots are offering service that exceeds the limits of their certifications"); United States v. Pierce, 785 F.3d 832, 841 (2d Cir. 2015) (First Amendment permits evidentiary use of speech to prove elements of a crime or motive or intent).

evidence that a drug is intended for a use that is not included on the drug's FDA-approved label."); United States v. Article of Drug Designated B-Complex Cholinos Capsules, 362 F.2d 923, 927 (3d Cir. 1966) (rejecting free speech challenge noting that there is "nothing new or alarming" in a ruling that statements may be taken as evidence of a party's intention).[9]

Amarin also reaffirms the role of truthful, non-misleading speech as evidence of intent where, as here, the Court's instructions require a non-speech criminal act. See Amarin Pharma v. FDA, 119 F. Supp. 3d 196 (S.D.N.Y. 2015). The court in Amarin stated: "The Government is of course correct that truthful speech can serve as evidence of intent." Id. at 228. Likewise, the Caronia court stated that FDA "regulations do recognize that promotional statements by a pharmaceutical company or its representatives can serve as proof of a drug's intended use." United States v. Caronia, 703 F.3d 149, 154–55 (2d Cir. 2012). The court noted: "The FDCA defines misbranding in terms of whether a drug's labeling is adequate for its intended use, and permits the government to prove intended use by reference to promotional statements made by drug manufacturers or their representatives." Id. at 162. Defendants' arguments to the contrary are counter to all precedent, and must continue to be rejected by this Court.

C. The Verdict Does Not Establish That All Speech Was Truthful and Non-Misleading and Evidence Established It Was Not.

As this Court's jury instructions recognize, false and misleading commercial speech is not protected by the First Amendment. Defendants incorrectly claim that the jury's acquittal of Defendants for the fraud or false and misleading labeling charges necessarily establishes that

[9] See also United States v. Cole, 84 F. Supp. 3d 1159, 1166 (D. Or. 2015); United States v. Regenerative Sciences, 878 F. Supp. 2d 248, 255-56 (D.D.C. 2012), aff'd, 741 F.3d 1314 (D.C. Cir. 2014); United States v. Livdahl, 459 F. Supp. 2d 1255, 1268 (S.D. Fla. 2005); United States v. Lane Labs-USA, 324 F. Supp. 2d 547, 579-80 (D.N.J. 2004); United States v. Gen. Nutrition, 638 F. Supp. 556, 562 (W.D.N.Y. 1986).

there was no false and misleading speech nor fraud by anyone. See Def. Mem. at 7-8. The failure of a jury to find, beyond a reasonable doubt, that these two Defendants had the requisite specific criminal intent to commit the frauds charged or that they caused the distribution of the device with false and misleading labeling, does not establish the opposite. See United States v. Seley, 957 F.2d 717, 723 (9th Cir. 1992) ("Instead of meaning that certain acts did not happen, an acquittal means that they were not proved beyond a reasonable doubt."). Acquitting the Defendants on these counts is not inconsistent with finding that Defendants, and/or others at Acclarent, committed a fraud upon the FDA or otherwise made false and misleading statements. For example, the good faith defense means that the Defendants could have been acquitted on the fraud counts simply because they misunderstood the law, even if the conduct violated the law. Dkt. 436 at 43 (jury instruction on good faith: "If a person acts either on a belief or an opinion honestly held that his actions were not criminal, that person's actions are not criminal simply because the belief or opinion turns out to be incorrect, inaccurate, or wrong.")

Moreover, the jury's verdict of acquittal on the false and misleading labeling theory of misbranding does not mean the jury found there was no false and misleading speech. Labeling, as the jury was instructed, must be "written, printed or graphic" and must meet other aspects of the statutory definition of labeling in the FDCA. Dkt. 436 at 28 ("Label and Labeling" jury instruction). There was ample evidence of false and misleading speech beyond the written labeling – including the oral statements of sales representatives and others.[10] The documents and witnesses described the following false and/or misleading claims, among others:

[10] See 5 Trial Tr. 159-160 (Vanderkarr: put her name on Elmore's slides to use with a surgeon for a presentation); 7 Trial Tr. 122-123 (Steffen: Elmore wanted representatives he supervised to use FESS by the Numbers, and the presentation was widespread in other territories); 11 Trial Tr. 84-85 (Bilsbury: gave FESS by the Numbers presentation more than

(1) that doctors would experience better outcomes/lower revision rates if they used Acclarent's tools and the Stratus for surgeries rather than other sinus surgery tools;[11]

(2) that doctors should use the Stratus with Kenalog with four, six or even eight devices in one patient in various sinuses, without any evidence of utility or safety at those dosages or locations, or warnings as to risks;[12]

(3) that the device could elute saline, or even Kenalog slowly and consistently over a period of 14 or 28 days,[13] when Acclarent's own Engineers as well as FDA reviewers had pointed out that evidence did not show this;[14]

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once and it improved his business); GX GX2284 (transcript of Steele Total Ostomy talk); GX2283_001 (audio of Steele Total Ostomy talk).

[11] See, e.g., 6 Trial Tr. 23-24 (Vanderkarr: never had data for lower revision rates as claimed in Steele talk); GX2284 at USA-003240 (transcript of Steele training reciting claims to doctors "We use a stratus technology that helps us finish off the case. As far as revision rates go, revision rates somewhere around 1.5%, 2% at all sinuses. That's really low compared to what is in the ectomy era."); id. at USA-003237 ("I only let my ostomy champions use a shaver for polyps . . . Everything else gets either ballooned or stratused, and we got the trust in the ostomy approach and I guarantee you it'll really work well for you.); id. at USA-003241 (recommending using Stratus to "elude[] out Kenalog over a month long period"); id. at USA-003244 (promising results will be better); 8 Trial Tr. 124-125 (Chong: Logan described Stratus as device "where medication could be placed in which would slowly allude over time in the sinus to help prevent polyp regrowth and prevent scarring); 9 Trial Tr. 98 (Convery: explaining how he describes Stratus as ideal for patients with polyps or inflammation because it would reduce the inflammation and make the polyps go away). 10 Trial Tr. 39 (Krinsky: Elmore presentation positioned Stratus to physicians "as an answer for patients postoperatively to improve the overall outcomes"); 10 Trial Tr. 108 (Logan: relaying how sales reps at national sales meeting described how they sold device); 11 Trial Tr. 72-73 (Bilsbury: explaining Fabian talk track for Stratus as step in process "for treating all frontal sinuses").

[12] See 6 Trial Tr. 117-22 (Steffen: sales representatives and managers Jason Elmore and Bob Block recommended selling / implanting six Stratus at one time); GX2284 at 3 (Steele transcript describing putting between four and seven Stratus into patient).

[13] See GX1279 at ACC-040-0767169 (script for sales reps to answer objections: "How do I know the saline will bathe the ethmoid over a 14 day span? The mechanics of the device are simple. The device is implanted into the ethmoid sinus and the reservoir is then filled to capacity. The reservoir material is crowded with micro-pores across its entire surface and they serve to wick out the saline over its programmed 2 week span."); 5 Trial Tr. 132-133 (Vanderkarr: did not believe above explanation to be true if device used with saline).

[14] See GX 2471 at p. 5 (IDE Disapproval Letter: ""We do not agree with your statement that your invitro elution requirements demonstrate the ability of the spacer membrane to control

(4) that all of Acclarent's devices, including Stratus, were "proven safe and effective" [15] even though evidence demonstrated, and Acclarent's own label for the device conceded, from late 2010, that Stratus had never been shown to be safe and effective with an active drug substance; [16] and

(5) that there were no adverse events with Acclarent products and/or only one adverse event with the Stratus,[17] despite Acclarent's own studies recording multiple adverse events in limited patient populations.[18]

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drug release over an extended period of time. The data you provide demonstrate very high variability in the amount of drug being released in 24 hours and you provide no data for beyond 24 hours."); 19 Trial Tr. 70 (Michele re: GX 2471: "So, they had some data in the laboratory. They didn't have data in humans, but they had some data in the laboratory that showed that only over the first 24 hours, and we thought that it showed that if you tested multiple devices, you got varying levels of drug out."); 19 Trial Tr. 36 (Michele: "it wasn't entirely clear because the elution profile of the drug from the device was never fully defined by the sponsor. So, we … had to make some calculations based on guessing that it came out at a steady state the entire 30-day period, but we were never really shown that."); GX415 (Ketan Muni: "As we are not releasing saline over 14 days, we should take that statement out.").

[15] See GX2506 at ACC-043-0162611-12 (Training slides claiming Stratus and other products were proven safe and effective); 5 Trial Tr. 65-67 (Vanderkarr: describing Acclarent "mantra" that all products, including Stratus, were described to physicians as "proven safe, proven effective, proven patient friendly); 7 Trial Tr. 41 (Vanderkarr: knew FDA had not determined if Stratus was safe and effective when used to deliver Kenalog); GX1428 at ACC-044-0000739 (Elmore discussing Stratus with Kenalog: "the benefits to you as a surgeon are a safe and effective tool).

[16] See GX2586 (Product Label: The safety and effectiveness of this device with an active drug substance in the reservoir have not been established."); 19 Trial Tr. 105 (Michele: Acclarent never gathered evidence to support safety and efficacy of Stratus to deliver Kenalog-40); 19 Trial Tr. 199-200 (Citardi: AAO clinical data on Stratus was inconclusive); 16 Trial Tr. 41-44 (Khan: there were multiple adverse events reported in Spacer study but not all were conveyed to FDA).

[17] See 6 Trial Tr. 37 (Vanderkarr: she did not recall providing any information to physicians regarding Stratus adverse events); 7 Trial Tr. 125-26 (Steffen: he gave FESS by numbers which identified only one adverse event regarding Stratus); 10 Trial Tr. 144 (Logan: describing GX1734, a document Convery used to "boost Stratus support," which identified that there were "no adverse events reported"); GX1734 at 4 (no adverse events reported); GX1428 (no adverse events and perfect safety record: GX1428 at ACC-044-0000732 (Elmore Fess by Numbers transcript: "yet to be an adverse event reported"]); GX1428 at ACC-044-0000733 (Elmore transcript: "literally we do not an adverse event in four years").

Several physicians also testified that these statements and omissions were material to them in their prescribing decisions.[19] Even defense witness Dr. Hoisington testified that he was never told that the saline ran right out or that liquids other than Kenalog eluted rapidly, and that this information would have been important to him in deciding how to use the Stratus.[20] Thus, there was clear evidence of false statements, and misleading statements that omitted material information, from which the jury properly could have found false and misleading speech. Ultimately, however, the jury was instructed that it could not convict based upon truthful, non-misleading speech alone. Thus, the jury may have found speech that was false or misleading, or relied upon evidence other than truthful speech to find intended use, or both. In either event, there is no constitutional issue.

D. The FDCA's Misbranding and Adulteration Provisions as Applied in this Prosecution of Defendants Survive First Amendment Scrutiny.

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[18] See 20 Trial Tr. 27-28 (Michele: Acclarent IDE filing noted six adverse events between February 2009 and July 2010); 19 Trial Tr. 48 (Michele: a number of adverse events were reported in Acclarent's annual reports on the SPACER study); 52 (Michele: 50 percent of patients in 14-patient SPACER study developed infection, according to spreadsheet); GX2537; 16 Trial Tr. 42 (Khan: underlying documents from SPACER study revealed more than the one adverse event reported in study, including headache, infection, migration of the device to the sphenoid sinus, and difficulty removing the device); 44 (Khan: documents relating to SPACER study reveal that approximately half of patients developed infection); 80 (Khan: DELIVER annual report from 2009 reported headaches, facial discomfort, and excessive pain)

[19] See, e.g., 3 Trial Tr. 142-51 (Armstrong: explaining it would be important and significant to know about adverse events or device malfunctions); 18 Trial Tr. 197-98 (Dr. Hwang: explaining it was "important" to know how much drug was getting into the tissues).

[20] See 22 Trial Tr. 141-142 (Hoisington: failure to wick out over 14 days would be significant if he were using with saline); 22 Trial Tr. 127-129 (Hoisington: reviewing prior testimony stating that he should have been told that most common antibiotics would wash out very rapidly; that such information was relevant to "making his clinical decisions").

Because Defendants were not charged with any speech crime, there is no need for further First Amendment analysis. The Court also need not reach the First Amendment analysis under Central Hudson Gas & Elec. v. Public Serv. Comm'n of N.Y., 447 U.S. 557, 566 (1980), or at least beyond the first step of that analysis, for other reasons. First, under the first step of Central Hudson, the First Amendment does not protect commercial speech that is false or misleading. See id. at 563. As noted above, the Government presented significant evidence to the jury that could support a conclusion that Defendants caused the distribution of the Stratus for unapproved uses in part by employing or failing to prevent false and misleading speech. Also, and also under the first step of Central Hudson, commercial speech that proposes illegal activity also enjoys no First Amendment protection. Id. Here, the jury's findings indicate that the jury found that the distribution of the device was, throughout the relevant time-period, illegal and intended for a use for which it was neither cleared nor approved. Acclarent's conduct in putting on the market a product that was never intended for its approved use and instead intended solely for an unapproved use was unlawful and thus speech in furtherance of that crime is simply not protected. See Caputo, 517 F.3d at 940-41 ("So the large Plazlyte, with its expanded "intended use", was not covered by the FDA's approval of the small Plazlyte and could not lawfully be sold *at all*…There was no lawful activity for speech to promote"); United States v. Cole, 84 F. Supp. 3d 1159, 1166 (D. Or. 2015) ("Both because Defendants' speech is being used as evidence of their intent and because it concerns illegal activity, the First Amendment is not violated.").

Nevertheless, even if the Court were to reach the remaining steps under the Central Hudson test, the FDCA and the implementing regulations challenged here survive First

Amendment scrutiny because they advance a substantial public interest, and are no more extensive than necessary to serve that interest. See Cent. Hudson, 447 U.S. at 566.[21]

1. The Government Has a Substantial Interest in Requiring Review of Medical Products for Their Intended Uses *Before* They Are Marketed and Distributed to Patients for Those Uses.

Preserving the effectiveness and integrity of the premarket clearance and approval processes for medical products serve an important governmental interest in protecting public

[21] This standard does not require the government to employ "the least restrictive" regulatory means, nor to achieve a perfect fit between means and ends. See Bd. of Trustees of State Univ. of NY v. Fox, 492 U.S. 469, 480 (1989). It is satisfied "so long as the . . . regulation promotes a substantial government interest that would be achieved less effectively absent the regulation." United States v. Albertini, 472 U.S. 675, 689 (1985).

Defendants erroneously assert that the First Amendment forbids the premarket review requirements as speaker- and content-based constraints on commercial speech, citing Sorrell v. IMS Health, 564 U.S. 552 (2011) and Reed v. Town of Gilbert, 135 S.Ct. 2218 (2015). Although the Supreme Court in Sorrell suggested in dicta that "heightened" scrutiny might apply to content-based restrictions on speech, it applied the Central Hudson test. Id. See 1-800-411Pain Referral Serv. v. Otto, 744 F.3d 1045 (8th Cir. 2014) (because Sorrell did not define heightened scrutiny, the Central Hudson test applies to restrictions on commercial speech that are content- or speaker-based); see also Mass. Ass'n. of Private Career Schools v. Healey, 159 F. Supp. 3d 173, 190–91 (D. Mass. 2016) (rejecting argument that Sorrell precludes the application of intermediate scrutiny as "the proper test for content-based restrictions on commercial speech") However, even if there were a "heightened" standard to apply, the FDCA restrictions are permitted because they directly advance substantial health interests, and there is no alternative that can demonstrably do the same.

Reed has no bearing here. In Reed, the Court applied strict scrutiny to content-based restrictions on non-commercial speech in public fora. Central Hudson supplies the appropriate test for the commercial speech at issue here, as recently noted by the court in Healey. See 159 F. Supp. 3d 173, 190–94 ("Although only a small number of courts have addressed First Amendment challenges to commercial-speech regulations since Reed, almost all of them have concluded that Reed does not disturb the Court's longstanding framework for commercial speech under Central Hudson."). See also San Francisco Apt. Ass'n v. City & Cnty. of San Francisco, 142 F. Supp. 3d 910, 922 (N.D. Cal. 2015); Chiropractors United for Research & Educ. v. Conway, 2015 WL 5822721, at *5 (W.D. Ky. Oct. 1, 2015) (appeal pending) ("Because the [challenged] [s]tatute constrains only commercial speech, the strict scrutiny analysis of Reed is inapposite."); Calif. Outdoor Equity Partners v. City of Corona, 2015 WL 4163346, at *10 (C.D. Cal. July 9, 2015) ("Reed does not concern commercial speech, let alone bans on off-site billboards. The fact that Reed has no bearing on this case is abundantly clear from the fact that Reed does not even cite Central Hudson, let alone apply it." (emphasis deleted)).

health and safety. See Thompson v. W. States Med. Ctr., 535 U.S. 357, 369 (2002). The government interests in protecting and promoting the public health are substantial. The products FDA regulates have the potential to adversely impact public health and safety. The FDCA of 1938, which introduced the requirement that firms demonstrate a product's safety before distributing it, followed the deaths of approximately 100 people from ingesting "Elixir Sulfanilamide," in which the lethal substance diethylene glycol was used as a solvent. The 1962 drug amendments, which require a showing of effectiveness, were precipitated in part by the distribution of thalidomide, a sleeping pill that caused birth defects when taken by pregnant women. See Wallace F. Janssen, Outline of the History of U.S. Drug Regulation and Labeling, 36 Food Drug Cosm. L.J. 420 (1981); Att. A, Declaration of Robert Temple, MD at ¶¶ 4-5, Allergan v. United States, 1:09-cv-01879 (D.D.C. Dec. 11, 2009), Dkt. 18.

The Medical Device Amendments of 1976 were also a response to public health tragedies, including from the Dalkon Shield intrauterine contraceptive device (IUD). See H.R. Rep. No. 94-853, at 8 (1976) (listing reports of at least 16 deaths, 25 miscarriages, and many cases of pelvic perforation from IUD). Such events also included significant defects in cardiac pacemakers that led to 34 voluntary recalls of 23,000 units, and serious side effects following implantation of intraocular lenses, including vision impairment and the need to remove some patients' eyes. Id. Beyond the direct harms sometimes caused by medical products, the lost opportunity to select an effective treatment for the underlying disease is itself a harm that often cannot be fully remedied after it is incurred. See Att. B, Declaration of Janet Woodcock, MD at ¶ 8, Amarin Pharma v. FDA, 15 Civ. 3588 (S.D.N.Y. Jun. 23, 2015), Dkt. 52.

There is also a substantial government interest both in generating robust data that supports safety and effectiveness, and in ensuring that diagnoses and treatment decisions are not

made based upon unreliable or inaccurate data. Congress developed the premarket review framework for medical products in response to the public health tragedies noted above, and after determining that: (1) exclusive reliance on post-market remedies, such as enforcement actions for false or misleading labeling, is unacceptable as a public health strategy for medical products because it does not sufficiently prevent harm and injury to patients; and (2) safety and effectiveness must be evaluated for each marketed intended use of a medical product to prevent the harm that occurs when patients are prescribed or use ineffective treatments and to ensure that the benefits of an intended use outweigh its risks. See H.R. Rep. No. 94-853, at 5-8 (1976); S. Rep. No. 94-33, at 1-7 (1975); Att. B, Declaration of Janet Woodcock, MD at ¶ 8-9. The FDCA premarket review requirements help the public to obtain the benefits of these products while mitigating the risks.

These premarket review requirements thus advance substantial government interests in increasing the availability of therapies that have been demonstrated to be safe and effective and in preventing direct and indirect harm from products that are unsafe, ineffective, or unproven. See S. Rep. No. 94-33, at 2-6 (1975). When using a medical product for its FDA approved/cleared intended use, health care practitioners and patients can be assured that the decision to use the product is supported by robust premarket review of scientific data and other evidence, as determined by an independent scientific agency.[22] In contrast, a firm's distribution of an unapproved medical product or an approved/cleared medical product for an unapproved

[22] See, e.g., Kesselheim, A.S., J. Avorn, "Pharmaceutical Promotion to Physicians and First Amendment Rights," New England Journal of Medicine, 358:1727-1732, 2008. ("In the pharmaceutical market, determining whether a drug is safe and effective for an intended use can involve dozens of FDA scientists poring over extensive databases of studies in animals, toxicologic evaluations, and clinical trials. In essence, the Agency acts as a learned intermediary on behalf of prescribing physicians.").

use, has the potential to undermine these substantial public health interests.[23] An incomplete, biased, or manipulative presentation regarding an unapproved use may lead to unsafe, ineffective, or unnecessary use of medical products.[24] Furthermore, to the extent a firm can forego premarket review and market an unapproved product or an approved/cleared product for an unapproved use, the firm's incentive to conduct the necessary research and comply with the premarket review processes are likely to be substantially reduced. [25] Excluding clearly probative

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[23] See, e.g., Good, C.B., W.F. Gallad, "Off-Label Drug Use and Adverse Events, Turning up the Heat on Off-Label Prescribing," JAMA Internal Medicine, 176(1):63-64, 2016 ("Even in situations where an off-label indication has been studied, pharmacokinetics, drug-disease interactions, and other safety considerations are unlikely to have been studied systematically to the level required during the FDA drug approval process. Likewise, few clinicians have the time or the motivation to review evidence for those off-label indications to arrive at a balanced assessment of the risks and benefits to support the appropriate use of that drug"); Eguale, T., et al., "Association of Off-Label Drug Use and Adverse Drug Events in an Adult Population," JAMA Internal Medicine, 176(1):55-63, 2016 (summarizing study and concluding that unapproved use of prescription drugs is associated with adverse drug events, particularly where those uses lack strong scientific evidence in the form of at least one randomized controlled trial).

[24] See Avorn, J. et al., "Forbidden and Permitted Statements About Medications --Loosening the Rules," New England Journal of Medicine, 967:971-972, 2015. ("Considerable research shows that marketing can drive prescribing practices, which in turn can lead to adverse patient outcomes if those decisions are not evidence-based."); Kapczynski, A., "Free Speech and Pharmaceutical Regulation--Fishy Business," JAMA Internal Medicine, 176(3):295-296, 2016. ("To be effective, a company's marketing must also influence the prescribing patterns of physicians . . . [T]here is a strong and specific association between pharmaceutical marketing and physician behavior, independent of the evidence supporting the products."); Cardarelli, R., J.C. Licciardone, L.G. Tayloe, "A Cross-Sectional Evidence-Based Review of Pharmaceutical Promotional Marketing Brochures and Their Underlying Studies: Is What They Tell Us Important and True?," BMC Family Practice, 7(1):13, 2006. (pharmaceutical industry marketing to prescribing physician creates the potential for prescribing practices that may not benefit the patient, which contribute to escalating healthcare costs).

[25] See Eisenberg, R.S., "The Role of the FDA in Innovation Policy," Michigan Telecommunications and Technology Law Review, 13:2:345, 370, 2007 ("By requiring that firms conduct rigorous clinical trials before bringing their products to market and before making promotional claims for their products, the FDA plays an important structural role in promoting a valuable form of biomedical R&D that private firms are undermotivated to perform on their own."); Kesselheim, A.S., M.M. Mello, "Healthcare

categories of evidence of intended use from consideration would also undermine the significant public health protections advanced by the premarket review system.

The FDCA approval process serves to require scientific study and robust data on safety and efficacy *before* new treatments are introduced. Congress mandated that medical product manufacturers gather data from rigorous scientific studies by establishing scientific evidentiary thresholds for FDA to apply in reviewing and clearing or approving medical products. These scientific requirements developed over time, partly in response to conduct that led to public health tragedies and insufficient regulatory authority to prevent the harm from occurring. In enacting the 1962 amendments to the FDCA, Congress recognized that poorly conducted studies and anecdotal evidence do not provide adequate information to assess the risk/benefit profile of drugs necessary to protect and promote public health. See Cooper Laboratories v. FDA, 501 F.2d 772, 778 (D.C. Cir. 1973) ("The 'substantial evidence' requirement reflects the conclusion of Congress, based upon hearings, that clinical impressions of practicing physicians and poorly controlled experiments do not constitute an adequate basis for establishing efficacy."). As the

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Decisions in the New Era of Healthcare Reform: Prospects for Regulation of Off-Label Drug Promotion in an Era of Expanding Commercial Speech Protection," North Carolina Law Review, 92:1539, 1585, 2014 ("There [would] be no need for companies to design these studies to meet the FDA's standards for methodological rigor if the companies have no intention of submitting an application for approval of the new use but rather intend to use the study findings only in marketing communications. Companies [could] design studies in ways that maximize the chances of obtaining a desired result and select which studies to emphasize in promotional communications, ignoring others that do not support their promotional message."); Stafford, R.S., "Regulating Off-Label Drug Use--Rethinking the Role of the FDA," New England Journal of Medicine, 358:14:1427-1428 (2008) (Encouraging unapproved uses "undermines the incentives for manufacturers to perform rigorous studies--and instead subtly encourages them to game the system by seeking approval for secondary indications for which clinical trials are less complicated and less expensive. And off-label use may discourage evidence-based practice.").

Supreme Court noted in Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609, 619 (1973), in upholding the FDA's regulations defining the substantial evidence standard for drugs:

> Lower courts have upheld the validity of these regulations and it is not disputed here that they express well-established principles of scientific investigation. Moreover, their strict and demanding standards, barring anecdotal evidence indicating that doctors 'believe' in the efficacy of a drug, are amply justified by the legislative history. The hearings underlying the 1962 Act show a marked concern that impressions or beliefs of physicians, no matter how fervently held are treacherous. Congress surely has great leeway in setting standards for releasing on the public, drugs which may well be miracles or, on the other hand, merely easy money-making schemes through use of fraudulent articles labeled in mysterious scientific dress. The standard of 'well-controlled' investigations particularized by the regulations is a protective measure designed to ferret out those drugs for which there is no affirmative, reliable evidence of effectiveness. The drug manufacturers have full and precise notice of the evidence they must present to sustain their NDA's, and under these circumstances we find FDA hearing regulations unexceptionable on any statutory or constitutional ground.

Id. at 622. Without such restrictions, companies could simply make up a sham use for their devices similar to some device on the market to get 510(k) cleared, as the jury could have found Acclarent did here, and then market the device for any use, no matter how dangerous, and the entire system for protecting patients from unsafe medical devices would be undermined.

2. Application of the Adulteration and Misbranding Provisions of the FDCA to This Case Is Not More Extensive than Necessary.

The FDCA provisions challenged here are narrowly drawn to fit these substantial government interests in several respects and are not more extensive than necessary. As Congress has repeatedly determined, to meet FDA's goal of ensuring the availability of effective medical therapies and preventing harm to patients, the FDA must be empowered to act to prevent harm ***before*** the public is exposed to unnecessary risks. Requiring FDA to wait to act until patients are injured from medical products does not allow FDA to meet the goals Congress set. Moreover, to accomplish its mission, the FDA needs studies and data concerning proposed medical products, their intended uses, and the safety and efficacy of such uses.

As the evidence in this case demonstrates, individual healthcare providers and patients typically lack the tools, background, and specialized expertise in statistics, biomedical engineering, and other fields to conduct a thorough evaluation of the risks and benefits of a new intended use that even roughly approaches that provided by FDA's independent, unbiased review.[26] Physicians often do not have available data beyond their own limited patients, and cannot uncover or weigh the significance of the absence of a full disclosure of all relevant data, assuming they even had the time for review. Id. See Bates v. State Bar of Ariz., 433 U.S. 350, 383-84 (1977) (holding that limitations on advertising may be appropriate where the public lacks sophistication or a means of verifying information on a particular topic). Eliminating the approval requirement for each intended use beyond the first cleared or approved use would, therefore, undermine the substantial government interests in the premarket approval process, including incentivizing robust research and studies for new uses, and requiring independent and unbiased premarket safety and effectiveness review for each use. Nor would alternatives suggested by Defendants or their Amici meet these goals. See Att. B, Woodcock Decl. ¶ 42, et seq. For example, counterspeech could not incentivize the scientific studies necessary for such a review. Nor could it match the pervasive impact of billions of dollars spent on medical product advertising. Disclaimers cannot substitute for labeling that is developed after a thorough

[26] See, e.g., 15 Trial Tr. 21-23 (Hwang: explaining concept of evidence-based medicine); 18 Trial. Tr. 224 (Citardi: "the purpose of this article [DX2354] was to discuss evolving expectations within the medical community in favor of, or in support of the greater use of evidence-based medicine"); DX2354 (Marple, B.F. et al., Going to the Next Level: Health Care's Evolving Expectations For Evidence, Otolaryngol Head Neck Surg. 141(5):551-4, 2009); 22 Trial Tr. 106 (Hoisington: "FDA may love a double blind controlled randomized study. Everybody does. That's type 1 one evidence. Everybody goes with that."); 22 Trial Tr. 139 (Hoisington: conceding, in response to question about whether he'd determined what level of steroid could increase ocular pressure, that he does not "run a lab").

assessment of the data and information relating to the new use, which labeling would include specific directions and warnings. Studies have shown the limitations of disclosures in terms of consumer perception and understanding in certain contexts – limitations that may exact too great a cost when lives and health depend on their success.[27] As the Supreme Court explained in reversing the dismissal of a conviction of an individual for introducing adulterated drugs into interstate commerce,

> [b]alancing relative hardships, Congress has preferred to place it upon those who have at least the opportunity of informing themselves of the existence of conditions imposed for the protection of consumers before sharing in illicit commerce, rather than to throw the hazard on the innocent public who are wholly helpless.

United States v. Dotterweich, 320 U.S. 277, 285 (1943).

In contrast, the Central Hudson evaluation conducted by the Second Circuit majority in Caronia addressed only the constitutionality of the legal theory the Court concluded was presented in that case to the jury – that the FDCA prohibits and criminalizes all manufacturer promotional communications regarding unapproved uses. See 703 F.3d at 161-64, 166-69. This Court's instructions make it very clear that the charged statutory provisions in this case do not constitute a complete prohibition on all such communications.

The law imposes special duties and requirements on manufacturers of medical products because they create the risks and have knowledge or the ability to acquire knowledge relevant to product risk. See Dotterweich, 320 U.S. at 285; United States v. Park, 421 U.S. 658, 672 (1975) ("The requirements of foresight and vigilance imposed . . . are no more stringent than the public has a right to expect of those who voluntarily assume positions of authority in business

[27] See Christopher Robertson, When Truth Cannot Be Presumed: The Regulation of Drug Promotion Under an Expanding First Amendment, 94 B.U. L. REV. 545, 551 (2014).

enterprises whose services and products affect the health and well-being of the public that supports them."). In addition, any indirect marketing restrictions potentially associated with the use of promotional statements as evidence of intended use must be viewed in light of the substantial benefits associated with FDA review and approval processes. Indeed, where, as here, there are significant government interests in requiring firms to engage in the premarket review process before they distribute products for a new intended use, firm-centered marketing restrictions are most specifically tailored to address the interests at stake. It makes sense for these restrictions to apply only to the entities that are positioned to benefit from increased sales of their products – and not apply to conduct and communications of truly independent healthcare professionals and researchers who do not have that economic motivation. A broader, more speaker- or content-neutral approach – that, for example, restricted all communication about unapproved uses by both firms and others – would impact more speech and would be less well-tailored to the various government interests. Thus, focusing on firms who benefit from medical product sales is an appropriate way to tailor the impact on communications so that it is not more extensive than necessary. For these reasons as well, the application of the FDCA to Defendants' conduct in this case does not violate the First Amendment.

III. COURTS HAVE HELD THAT THE FDCA, ITS MISDEMEANOR PROVISIONS, AND INTENDED USE CONCEPT DO NOT VIOLATE DUE PROCESS.

A. The Controlling Authority Holds that the FDCA and Its Intended Use Provisions Are Not Unconstitutionally Vague.

The Supreme Court rejected due process challenges to the FDCA, and the misbranding and adulteration sections in particular, more than sixty years ago. See United States v. Sullivan, 332 U.S. 689, 695 (1948) (rejecting due process challenge to FDCA and finding no ambiguity in the misbranding language). The First Circuit also long ago summarily rejected such a vagueness

challenge to the FDCA. V.E. Irons v. United States, 244 F.2d 34, 45 (1st Cir. 1957) (rejecting as "untenable" the claim that the FDCA's misdemeanor misbranding provisions are unconstitutionally vague and upholding misbranding conviction for distribution of vitamin and mineral products shown to be intended for use as a drug.)

The Seventh Circuit in Caputo rejected a vagueness challenge to the device regulations specifically. Caputo, 517 F.3d at 936-37. The Caputo Court also held that the FDA's actual notice to the defendants precluded a vagueness argument. See also United States v. Reece, 2013 WL 5234124, at *8 (W.D. La. Sept. 13, 2013) (rejecting vagueness challenge to drug misbranding charge because of "notice provided in the statue, the regulations, and the extensive jurisprudence finding the FDCA is not unconstitutionally vague.); Att. C, United States v. Vascular Solutions, No. 14-CR-926-FB, Dkt. 128, Slip Op. at 6-7 (W.D. Tex. 2015) (citing cases) (rejecting vagueness challenge to charges of distribution of medical device for new intended use without required FDA clearance). Here also, the evidence demonstrated that Defendants had ample notice that the conduct for which they were convicted was prohibited.[28]

[28] See GX202 at ACC-002-00001390 (5/21/07 FDA Ltr. to Acclarent: "Based solely on the change or modifications that you have described, it appears that you have significantly changed or modified the design, components, methods of manufacture, device labeling or intended use of the device referenced above."); GX695 at ACC-201-0171411 (6/5/08 Acclarent S-1 signed by William Facteau: "If we materially modify our FDA cleared devices, we may need to seek and obtain new clearances, which, if not granted, would prevent us from selling our modified products. . . . Medical devices can be marketed only for the indications for which they are cleared or approved. After a device received 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a new or major change in its intended use, will require a new 510(k) clearance, or depending on the modification, pre-market approval."); GX1172 (Training slides provided to Defendants and sales force at 2009 National Sales Meeting: defining intended use (ACC-002-0000545), explaining that manufacturer can only sell products for cleared intended uses (ACC-002-0000549), explaining that training must be consistent with approved labeling (ACC-002-0000550), advising not to train doctors inconsistent with cleared indications (ACC-002-0000553), advising to only promote cleared products for "those uses cleared by FDA" (ACC-002-0000554), advising not to

As noted by the Court in General Nutrition in 1986, and still true today, "The [FDCA] on numerous occasions has been upheld against vagueness challenges – and this Court is unaware of any case holding any provision of the Act void for vagueness in any circumstance." 638 F. Supp. at 564. The Court explained:

> [T]he Act provides a clear, albeit complex, scheme designed to safeguard against the sale as medicine of products which may cause indirect harm by not living up to the promises made in connection therewith, or which may cause direct harm, or which are simply harmful *in potentia* because their effects have not been ascertained. . . . [I]t is not unreasonable to expect one in the business of selling any products for human consumption to recognize that lack of knowledge . . . has a potential for harm and may well be the subject of legislation.

Id.[29] Defendants and Amici cite no contrary case law.

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solicit or prompt customer questions regarding off label uses (ACC-002-0000555), advising not to initiate or solicit discussions about Stratus's use off label (ACC-002-0000565); GX1168 (Attorney Howard Holstein compliance slides circulated to Defendants and presented to at least Defendant Facteau explaining that a product is misbranded if it is marketed without first obtaining a 510(k) and is adulterated if it is marketed without first obtaining a PMA (Slide 4), explaining that training must be consistent with approved labeling (Slide 18), noting that unsolicited requests "can't be prompted" (Slide 23), advising "not" to "promote cleared … products for uses that are not cleared … by FDA" (Slide 30)); GX281 at slide 25 (9/11/07 Condor Project Approval: "Regulatory Assessment Summary – Do we currently have the required regulatory indication for the commercial launch? NO [in red]").

[29] See also United States v. Forester, 346 F.2d 685, 685 (4th Cir. 1965) (per curiam) (upholding provision deeming prescription drug to be misbranded if not dispensed pursuant to a prescription); United States v. Hohensee, 243 F.2d 367, 370 (3d Cir. 1957) (rejecting vagueness challenge to 21 U.S.C. § 351(f) and upholding, in context of second offense misdemeanor, conviction for distribution of misbranded products due to lack of adequate directions for use); United States v. 2600 State Drugs, 235 F.2d 913, 916 (7th Cir. 1956) (holding that misbranding provisions for products held for sale were not unconstitutionally vague and within Congress's authority to prohibit); United States v. Scully, 2015 WL 3540466, at *55 (E.D.N.Y. 2015) (noting that "Courts have repeatedly upheld the constitutionality of the misbranding provisions of the FDCA . . . in the face of vagueness challenges" (internal citations omitted)); United States v. Travia, 180 F. Supp. 2d at 115, 123 (D.D.C. 2001) (rejecting vagueness challenge to statutory provision stating that drugs are misbranded "if they fail to bear adequate directions and warnings," holding that "Congress has provided sufficient notice through [this provision]; [it is] not so vague or standardless that the ordinary public is left uncertain as to what is prohibited"); United States v. Carlson, 2013 WL 5125434, at *1, 10-11 (D. Minn. 2013) (rejecting vagueness challenge to FDCA misbranding provisions); Nat'l Assoc. of Pharma. Mfgs. v. HHS, 586 F.

B. Intended Use Concept Is Fundamental to the Entire FDCA Regulatory Scheme to Protect Patients from Unsafe Medical Products.

Moreover, the intended use concept that Defendants and their Amici challenge here is not just a product of long-upheld FDA regulations, 21 C.F.R. § 801.4 (devices) and § 201.128 (drugs, same language). It is fundamental to the statutory scheme itself, which, as discussed above, has been repeatedly upheld against such challenges. It is the intended use of a product that defines it as a medical device or drug in the first place, and the intended use is also the basis of every drug and device approval. 21 U.S.C. § 321(g) (definition of drug as item "intended for use in diagnosis, cure, mitigation, treatment or prevention of disease . . .."); § 321(h) (definition of device as "instrument . . . intended for use in the diagnosis of disease, or other conditions or in the cure, mitigation, treatment or prevention of disease . . ."). The intended use of a product is also fundamental to the required evidence of safety and efficacy. A product safe and effective for the intended use as a toenail clipper may not be safe or effective for the intended use as a tool to clip blood vessels in brain surgery.

Defendants' argument that the intended use concept – which permeates the entire FDCA – violates due process would undermine the entire statutory scheme which lies at the heart of the nation's comprehensive consumer protection system for food and medical products. The Supreme Court and other courts, however, have repeatedly upheld the intended use concept as the linchpin of the statutory requirements. See Weinberger v. Hynson, Westcott & Dunning, 412

Supp. 740, 754 (S.D.N.Y. 1984) (recognizing Supreme Court rejected a vagueness challenge to misbranding provisions).

U.S. 609 (1973) (explaining FDA is not to approve a new drug without "substantial evidence" that the new drug is "effective for its intended use.").[30]

In addition, 21 C.F.R. § 801.4 does not proscribe conduct or expression. It interprets the term "intended use" referenced in the statutory definition of "device" (21 U.S.C. § 321(h)), and applicable to statutory and regulatory provisions relevant here. See, e.g., 21 C.F.R. 807.81(a)(3) (requiring new premarket notification when cleared device "is about to be significantly modified in design components, method of manufacture or intended use"). If this "broad statutory requirement . . . is not excessively vague, certainly the instant regulations, which refine and interpret that requirement, are not unlawful." Nat'l Assoc. of Pharma Mfgs. V. HHS, 586 F. Supp. 740, 754 (S.D.N.Y. 1984) (rejecting vagueness challenge to FDA adulteration regulations requiring compliance with current good manufacturing practices).[31]

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[30] See also, e.g., United States v. Storage Spaces Designated Nos. 8 & 49, 777 F.2d 1363, 1366 (9th Cir. 1985) ("The vendor's intent is the key element in this statutory definition."); Nat'l Nutritional Foods Ass'n v. Mathews, 557 F.2d 325, 333 (2d Cir. 1977) ("The vendors' intent in selling the product to the public is the key element in this statutory definition." (citing cases back to 1952)); Cole, 84 F. Supp. 3d 1159 (same). See generally Reece, 2013 WL 5234124, at *7–8) (noting that the intended use regulation for drugs, "pertaining to labeling obligations has been a part of the law" since February 1976 repeatedly held not to be vague); 21 U.S.C. § 393(b)(2) (1994 ed., Supp. III) (defining the FDA's mission); More information for Better Patient Care: Hearing before the Senate Committee on Labor and Human Resources, 104th Cong., 2d Sess., 83 (1996) (statement of FDA Deputy Comm'r Schultz) ("A fundamental precept of drug and device regulation in this country is that these products must be proven safe and effective before they can be sold."); 21 U.S.C. § 393(b)(2) (1994 ed., Supp. III) defined the FDA's '[m]ission to include "protect[ing] the public health by ensuring that . . . drugs are safe and effective and that 'there is a reasonable assurance of the safety and effectiveness of devices intended for human use.").

[31] Nor have Defendants offered any valid reason why there is a potential for discriminatory enforcement here. See Gen. Nutrition, 638 F. Supp. 556, 560-61 (rejecting challenge to the FDCA based upon a potential for arbitrary enforcement as without basis); Carlson, 2013 WL 5125434, at *10-11 (holding such a challenge lacked sufficient showing that any of the provisions at issue permit arbitrary and discriminatory enforcement").

Nor does the fact that the statutory scheme is complex or requires thought to craft appropriate instructions render it unconstitutional. "The mere fact that a statute or regulation requires interpretation does not render it unconstitutionally vague." United States v. Lachman, 387 F.3d 42, 56-57 (1st Cir. 2004). As the First Circuit explained in Lachman, in overturning the district court ruling that the regulation there was void for vagueness:

> Many statutes will have some inherent vagueness. . .. Even trained lawyers may find it necessary to consult legal dictionaries, treatises, and judicial opinions before they may say with any certainty what some statutes may compel or forbid. This is particularly the case where, as here, the statute deals with economic regulation and is addressed to sophisticated businessmen and corporations which, because of the complexity of the regulatory regime, necessarily consult counsel in planning their activities, and where an administrative process exists to secure advisory interpretations of the statute.

Id. (citations omitted).[32] The due process challenges of Defendants and their Amici do not address the facts of this case and are foreclosed by controlling authority.

C. This Court Correctly Rejected Claim That Only External Marketing Statements Can Serve As Evidence of Intended Use.

Defendants are also incorrect in their argument that only external marketing claims may be considered as evidence of intended use. As this Court recognized with its instructions, there is no authority for such a limitation on the jury's consideration. Such a limitation is contrary to the plain language of the regulation, significant case law and common sense.

The language of the regulation defining intended use explicitly permits it to be determined by, among other things, "the circumstances surrounding the distribution of the

[32] See also United States v. Iverson, 162 F.3d 1015, 1021 (9th Cir. 1998) (rejecting vagueness challenge to Clean Water Act by convicted chemical company president and noting that "where, as here, a criminal statute regulates economic activity, it generally 'is subject to a less strict vagueness test, because its subject matter is more often narrow and because businesses can be expected to consult relevant legislation in advance of action.'").

article." 21 C.F.R. 801.4(d). The regulation also makes clear that intended use may be shown by evidence other than external marketing claims by stating that it "may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised." Id.

In addition, the dichotomy Defendants seek to create – between external marketing claims and the design and function of the device – simply does not exist in this case. The evidence here amply demonstrated that Defendants caused the distribution of the Stratus for drug delivery by making external marketing claims that it was specifically designed to deliver the thick liquid that was Kenalog-40 and that it could not reliably and slowly elute the thin liquid that is saline – the approved use.[33] This claim was explained by the very first witness, Dr. Armstrong, and repeated by nearly every sales representative in the context of how they were trained and how they explained the product, as well as in the Elmore recording.[34] Wendy Oakes testified that this was explained to the physicians on the Scientific Advisory Board as well.[35] It was stated in the sales representative discussion guide as an answer to a question.[36] Moreover, the one glossy sales brochure that sales representatives were given to show to potential users depicted the Stratus with a thick, white fluid bubbling out of its pores. GX1140, GX2424

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[33] See supra nn. 4-6 (describing documents and testimony from Acclarent sales representative explaining how Stratus did not work with saline).

[34] See 3 Trial Tr. 61-63 (Armstrong: Dr. Hoisington told him at Sinus forum that holes were specifically designed for Kenalog); see also supra nn. 4-6.

[35] See 7 Trial Tr. 167-68 (Oakes: SAB members described saline "run[ing] out very rapidly because those pore sizes would not have been designed to work effectively with saline")

[36] See GX706 at ACC-034-0004111 ("Our testing demonstrates that most common antibiotics would wash out of the device very rapidly").

(Stratus sell sheets). Acclarent's Strategic Marketing Director Dan Harfe, confirmed that the liquid in the picture was, in fact, Kenalog. GX849. Thus, reference to the design of the product – its purpose, its function, and the physical characteristics of its holes – to elute a liquid over time only if that liquid had the viscosity of Kenalog-40 was in fact an external marketing claim.

In addition, for at least half a century, Courts have made clear that evidence other than external marketing claims may be relevant to a determination of intended use of a medical product and that such evidence may come from "all relevant sources" including items such as the nature of the chemical involved, consumer use patterns, functionality of product, or distributor knowledge as to an unapproved use. See V.E. Irons, 244 F.2d at 44 ("[W]e are free to look to all relevant sources in order to ascertain what is the 'intended use' of a drug, and are not merely confined to the labels on the drug or the 'labeling.'"); Nature Food Ctrs. v. United States, 310 F.2d 67, 70 (1st Cir. 1963) ("It can hardly be thought that in offering such esoteric products [certain chemicals]. . . , which, among others, were described on the bottle as "need in human nutrition not established,' defendant had no special purposes in mind.").[37] The legislative

[37] See also Storage Spaces, 777 F.2d at 1366, n. 5 ("self-serving labels cannot be allowed to mask the vendor's true intent as indicated by the overall circumstances"); United States v. An Article of Device Toftness Radiation Detector, 731 F.2d 1253, 1257 (7th Cir. 1984) (intended use established in part by testimony that device used to treat patients); ASH v. Harris, 655 F.2d 236, 240 (D.C. Cir. 1980) (If consumers "use the product predominantly—and in fact nearly exclusively—with the appropriate intent . . . [,] the requisite statutory intent can be inferred."); Nat'l Nutritional Foods Ass'n v. Weinberger, 512 F.2d 688, 703 (2d Cir. 1975) (intended use as drug could be inferred from near exclusive consumer use of vitamins at certain levels for therapeutic purposes, and lack of recognized nutritional use); United States v. Article of 216 Cartoned Bottles, "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, . . . and any other relevant source."); LeBeau, 2016 WL 447612, *8 (same); United States v. Carlson, 2013 WL 5125434, at *6-7 ("[T]here is nothing "novel" about prosecuting someone for mislabeling a drug labeled as "not for human consumption" when in fact consumption was precisely the drug's alleged intended use, further alleged to be known and intended by the Defendant."); Regenerative Sciences, 878 F. Supp. 2d at 255-56 (any relevant source); United States v. Sybaritic, 789 F. Supp. 2d 1160

history of the statute also supports this approach. See, e.g., H.R. Rep. No. 94–853, at 14 (1976) (FDA may consider "actual use of a product in determining whether or not it is a device.").

The Court in Vascular Solutions explained why it makes no sense that evidence of intended use does not include evidence of internal statements. The Court stated:

> [T]hough § 801.4 indeed says that "objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives," nowhere does the regulation state that such statements or claims cannot be used to show objective intent unless they were published to the marketplace. To see the absurdity of defendants' argument, consider a hypothetical in which a medical device manufacturer sells device D, which is approved for use A but frequently prescribed by doctors for off-label use B. If the manufacturer creates a bumper sticker with the words "I intend D to be used for B: Prescribe D for B Today," by defendants' logic that poster is inadmissible evidence of subjective intent so long as it sits in his briefcase, but admissible evidence of objective intent once he sticks it on his car. The Court is not persuaded that there is a legally relevant distinction here; in either scenario, the defendant has manifested into the physical world "oral or written statements" that may be weighed as evidence of objective intent.

Att. D, Vascular Solutions, 14-CR-926 (W.D.T.X., Jan. 26, 2016) (Dkt. 213 at 7).

The Court in United States v. Travia, 180 F. Supp. 2d 115, 119 (D.D.C. 2001), likewise applied these principles to hold that intended use could be demonstrated by the totality of the circumstances surrounding the sale of the drug in that case – nitrous oxide (laughing gas) – "namely, the selling of balloons of laughing gas in the parking lot at a rock concert." The court

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(D. Minn. 2011) (same); United States v. 250 Jars U.S. Fancy Pure Honey, 218 F. Supp. 208, 211 (E.D. Mich. 1963) (same), aff'd., 344 F.2d 288 (6th Cir. 1965); United States v. Ten Cartons Ener–B Vitamin B–12, 72 F.3d 285, 287 (2d Cir. 1995) (holding that something can be a drug for reasons other than claims made in labeling, such as "method of intake"); United States v. Kasz Enterprises, Inc., 855 F. Supp. 534, 539 (D.R.I. 1994) (intended use may be shown by "evidence that the vendor is aware that his product is being offered or used by others for a purpose for which it is neither labeled nor advertised."), modified on other grounds, 862 F. Supp. 717 (D.R.I. 1994); United States v. 789 Cases Latex Surgeons' Gloves, 799 F. Supp. 1275, 1285, 1294–95 (D.P.R. 1992) (intended use shown by all facts, including "actual use").

there rejected defendants' argument that because they had made no representations in labeling and advertising the balloons, they could not be selling a drug under the FDCA. The Court stated:

> The Court can find no support for the defendants' position. Labeling is not exclusive evidence of the sellers' intent. Rather, as the very language quoted by the defendants themselves states, "it 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'. . . even consumer intent could be relevant, so long as it was pertinent to demonstrating the seller's intent .... [I]f the government's allegations are true, the sellers did not need to label or advertise their product, as the environment provided the necessary information between buyer and seller.

Id. at 118-119 (citations omitted).

Similarly, the Seventh Circuit in Caputo upheld the conviction where design features were part of the evidence of intended use. There, the district court recited evidence of the differences in design of the cleared and uncleared device: "The larger sterilizer had different design and engineering characteristics: a six cubic foot chamber; a 5% peracetic acid mixture; different temperature, pressure, and gas flow rate; and a single, as opposed to multiple, use of the sterilant." United States v. Caputo, 456 F. Supp. 2d 970, 973 (N.D. Ill. 2006), aff'd in part, vacated in part, remanded, 517 F.3d 935 (7th Cir. 2008).

Nor, contrary to Defendants' claim, is there any absurdity created by reading the plain language of the statute and regulation to mean what it says. Permitting the jury to hear evidence of internal design plans in no way means that the jury must conclude that those plans evidence the intended use of the currently distributed product. Defendants remain free to argue or offer evidence that such plans were for a future product, and did not reflect the intended use of the product in commercial distribution. But there was ample evidence at trial that the design plans

did not reflect designs for a future additional use.[38] The evidence, which the jury could credit, was that by designing the hole size large enough for the unapproved use – to elute Kenalog over the implantation time, Acclarent necessarily impeded the function of the device for the claimed and cleared use, as a saline inflated and eluting spacer, because the saline would run right out.[39]

Also, United States v. Articles of Drug for Veterinary Use, 50 F.3d 497, 500 (8th Cir. 1995) does not hold that internally maintained product literature cannot be evidence of intended use. In fact, the court held that the materials maintained within the manufacturers' facility, were *properly* submitted to the jury for consideration in determining the intended use of the product – even absent evidence they were ever used externally to promote the products. Id. at 501.[40]

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[38] See GX72 at ACC28-0028364 (January 2006 Product Specification for Stratus (7 Trial Tr. 74) identifying "Key Requirement" as "ability to inject Kenalog" and "ability to contain Kenalog 40 for . . . at least 14 days;" signed by Facteau); GX259 at ACC28-0040856 (8/13/07 Condor Project Charter: "The CONDOR Sinus Spacer is a system of devices designed to locally deliver a pharmacologic agent to the paranasal sinuses with sustained-release capabilities. . ."); GX281 at slide 4, slid 16 (9/11/07 Condor Project Approval: "This presentation focuses on an Ethmoid drug delivery product"; "Goal: Commercially launch a drug delivery product for the Ethmoid as quickly as possible."); GX346 at ACC-011-0000252 (10/17/07 Condor Meeting Minutes: "CONDOR . . . comprises a system of devices designed to locally delivery a pharmacologic agent…. The project goal is to get a safe device into as many surgeons' hands as quickly as possible and gather data ….").

[39] See supra nn. 4-6.

[40] Defendants continue to mistakenly rely upon Brown & Williamson Tobacco v. FDA, 153 F.3d 155, 163 (4th Cir. 1998), aff'd. on other grounds, 529 U.S. 120 (2000) but the Fourth Circuit merely noted, in otherwise concluding that tobacco is not a drug or device subject to the FDA's jurisdiction, that there was no case where intended use has been found "absent manufacturer claims as to that product's use." Id. In fact, one year later, the Court in Travia held that nitrous oxide could be found to be intended for use as a drug without evidence of any external labeling, because the circumstances of its distribution in rock concert parking lots demonstrated its intended use as a drug. 180 F.Supp.2d at 118-119. Defendants also rely upon a letter from former FDA General Counsel Daniel Troy. Dkt. 185, Ex 1. That letter, however, addresses a situation where there were no external marketing claims, which distinguishes it from this case. Id. Nor could such a letter alter the plain meaning of the regulations. The letter is not an advisory opinion or formal guidance, the only two methods, short of rulemaking, for FDA to

D. Evidence of "Probing Questions" Was Appropriate.

Defendants' claim that the FDCA is unconstitutional because the safe harbor concept of 'unsolicited" is unclear is likewise without merit. See Def. Mem at 21-22. The conduct of conviction here was the distribution of the misbranded and adulterated device. Evidence of "probing questions" designed to lead the physician to discuss use of the device for drug delivery was just another way of demonstrating the actual intended use of the device.

Nor did these questions even come close to falling within the FDA's safe harbor for truthful, balanced, non-misleading, non-promotional responses to unsolicited requests for scientific information. The evidence of "probing questions" in this case was not truthful, balanced responses to scientific questions, but questions used as part of their promotional pitches, pitches so clearly designed to encourage doctors to ask about drug delivery that the sales force joked they should just wear pins that said "Ask me about Kenalog." 4 Trial Tr. 193-94 (Vanderkarr: joked about "Ask me about Kenalog" pin).

More fundamentally, a defendant is not entitled to a list of all of the types of evidence that may be used to show an element.

> A criminal statute must be sufficiently definite to give notice of the required conduct to one who would avoid its penalties, and to guide the judge in its application and the lawyer in defending one charged with its violation. But few words possess the precision of mathematical symbols, most statutes must deal with untold and unforeseen variations in factual situations, and the practical necessities of discharging the business of government inevitably limit the specificity with which legislators can spell out prohibitions. Consequently, no

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announce policies of general applicability. See 21 C.F.R. § 10.85(a)-(c) (advisory opinions); 21 U.S.C. § 317(h) (guidance); 21 C.F.R. § 10.115(f)-(g) (guidance); 21 C.F.R. § 10.85(k) (communication from an FDA employee that does not meet the requirements of an advisory opinion does not "represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed"). Nor do any of the other cases cited by Defendants and their Amici actually hold that, contrary to the language of the regulation, no evidence other than external marketing materials is permitted to demonstrate intended use.

> more than a reasonable degree of certainty can be demanded. Nor is it unfair to require that one who deliberately goes perilously close to an area of proscribed conduct shall take the risk that he may cross the line.

Boyce Motors v. United States, 342 U.S. 337, 340 (1952).

Defendants understood that the Stratus was not FDA approved for drug delivery and, the evidence demonstrated and the jury could have found, they nonetheless put it on the market for precisely and solely that purpose. This was clearly illegal. There is no constitutional infirmity or unfairness from this prosecution.

E. Lack of a Scienter Requirement Does Not Make an Otherwise Unambiguous Statute Unconstitutionally Vague.

Defendants' argument that the lack of a mens rea requirement in the misdemeanor provision of the FDCA "compels" the conclusion that their convictions violate due process is also foreclosed by precedent.[41] As discussed earlier, the First Circuit has already held, in upholding a misdemeanor misbranding conviction, that the FDCA is not unconstitutionally vague in V.E. Irons, and it did so after explicitly acknowledging that "one may be guilty of the misdemeanor described in 21 U.S.C. § 333(a) without having any intent to defraud or mislead." 244 F.3d at 43, 45. In Park, 421 U.S. at 666, 673, the Supreme Court reversed an appellate court decision holding that due process required at a minimum proof that the defendant was not just an unwitting responsible corporate officer. In reversing the court of appeals in Park, the Supreme Court necessarily rejected the proposition that the Due Process Clause precluded a conviction without proof of scienter.

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[41] Cf. United States v. H. B. Gregory 502 F.2d 700, 706 (7th Cir. 1974) ("If the Supreme Court standards of individual criminal liability announced in Balint, Dotterweich and Wiesenfeld Warehouse, [] are to be set aside, we shall defer to the Court's collective wisdom in that area. We shall not undertake to overrule the Supreme Court.")

Moreover, the Supreme Court has long ago and repeatedly acknowledged that Congress may properly dispense with the mens rea requirement. As explained in United States v Balint, 258 U.S. 250, 251 (1922):

> While the general rule at common law was that the scienter was a necessary element in the indictment and proof of every crime, . . . there has been a modification of this view in respect to prosecutions under statutes the purpose of which would be obstructed by such a requirement. It is a question of legislative intent to be construed by the court. It has been objected that punishment of a person for an act in violation of law when ignorant of the facts making it so, is an absence of due process of law. But that objection is considered and overruled in Shevlin-Carpenter Co. v. Minnesota, 218 U. S. 57, 69, 70, 30 [], in which it was held that in the prohibition or punishment of particular acts, the state may in the maintenance of a public policy provide 'that he who shall do them shall do them at his peril and will not be heard to plead in defense good faith or ignorance.' Many instances of this are to be found in regulatory measures in the exercise of what is called the police power where the emphasis of the statute is evidently upon achievement of some social betterment rather than the punishment of the crimes as in cases of mala in se. [Additional citations omitted].

The Supreme Court in Morissette v. United States, 342 U.S. 246, 255-56 (1952) explained why statutes regarding public welfare offenses do not need any intent element:

> Many of these [public welfare offenses] are …. in the nature of neglect where the law requires care, or inaction where it imposes a duty. Many violations of such regulations result in no direct or immediate injury to person or property but merely create the danger or probability of it which the law seeks to minimize. . . . In this respect, whatever the intent of the violator, the injury is the same, and the consequences are injurious or not according to fortuity. Hence, legislation applicable to such offenses, as a matter of policy, does not specify intent as a necessary element. The accused, if he does not will the violation, usually is in a position to prevent it with no more care than society might reasonably expect and no more exertion than it might reasonably exact from one who assumed his responsibilities.

The Eighth Circuit also recently rejected the argument by two executives convicted of misdemeanor FDCA violations that their prison sentences violated due process due to the lack of a mens rea requirement. United States v. DeCoster, --- F.3d ---, 2016 WL 3615684, at *5 (8th Cir. July 6, 2016). In affirming the three-month prison sentences, the Court in DeCoster

observed that "the elimination of criminal intent under 21 U.S.C. § 333(a) did not violate due process because, as the Supreme Court explained, Congress has seen fit to enforce the accountability of responsible corporate agents dealing with products which may affect the health of consumers by penal sanction cast in rigorous terms." Id. at *5.[42]

Colautti v. Franklin, 439 U.S. 379, 393-94 (1979), relied on by Defendants, did ***not*** hold that a lack of a mens rea requirement rendered the abortion statute at issue vague. Colautti dealt with a statute requiring any person who performed or induced an abortion to make a determination "based on his experience, judgment, or professional competence" that the fetus was not viable. Id. at 391. The statute further required that, if a person determined that the fetus was "viable" or there was "sufficient reason to believe that the fetus may be viable," then the person must adhere to a specific standard of care. Id. at 391. The Court found the statute unconstitutionally vague because these requirements contained a "double ambiguity" as it was unclear: (1) how a physician should make the viability determination, and (2) whether the phrase "may be viable" referred to "viability" as described in Roe v. Wade or some "gray area prior to the stage of viability." Id. at 391. Contrary to Defendants' claim, Colautti did ***not*** hold that the "the absence of scienter rendered the vague provision 'void on its face.'" Def. Mem. 23-24. The

[42] Thus, while a scienter requirement can "mitigate a law's vagueness," a statute is not void for vagueness because it lacks a mens rea requirement. See Hotel & Motel Ass'n of Oakland v. City of Oakland, 344 F.3d 959, 973 (9th Cir. 2003) (rejecting contention, made pursuant to Coluatti, that the lack of a mens rea requirement renders a statute unconstitutionally vague: "[T]he [Supreme] Court has never suggested that the absence of a mens rea requirement, by itself, renders a statute unconstitutional"); United States v. Harris, 705 F.3d 929, 932 n.2 (9th Cir. 2013) (rejecting vagueness challenge to statute criminalizing having a concealed weapon and holding that the statute's "lack of a scienter element does not render it unconstitutionally vague"); Cf. Staples v. United States, 511 U.S. 600, 619 n.17 (1994) ("Certainly, we have not concluded in the past that statutes silent with respect to mens rea are ambiguous.").

Court explicitly stopped short of considering that question, holding that the statute's "viability determination provision" itself rendered it void:

> Because we hold that the viability determination provision of § 5(a) is void on its face, we ***need not now decide*** whether, under a properly drafted statute, a ***finding of bad faith or some other type of scienter*** would be required before a physician could be held criminally responsible for an erroneous determination of viability.

Id. at 396.

Defendants also contend that the lack of a mens rea is particularly relevant because, they claim, the evidence at trial established that Acclarent's regulatory team "clearly believed that probing questions were allowed under FDA rules" and that the jury convicted Defendants despite there being "no evidence" that Defendant sought to undermine the direction from Acclarent's regulatory team. Def. Mem. at 24. They are wrong both as a matter of law and fact.

First, as a matter of law, even if Acclarent regulatory personnel were misinformed as to the regulations, that would not render those regulations void for vagueness. Moreover, to the extent that any regulatory personnel understood but chose to ignore the law and regulations, that is also irrelevant to the constitutional analysis. See, e.g., GX 849 (email informing Regulatory VP, *prior* to full launch with that sell sheet, that picture in sell sheet was Stratus filled with Kenalog); GX2424 (Stratus sell sheet).

In fact, however, the evidence demonstrated that Defendants received and undermined two detailed compliance presentation from the regulatory team and an outside lawyer, both of which made clear that employees should "NOT solicit or prompt customer questions regarding

off-label uses."[43] Also, Defendant Facteau attended a presentation, before the launch of the Stratus, from regulatory and project team, which clearly stated that the company did not have the required FDA approval for the Stratus – by putting a red box, like a stop light, with the word "NO" in answer to the question "Do we currently have the regulatory indication required for the commercial launch?" GX 281 at slide 25 (9/11/17 Condor Approval slide, 12 Trial Tr. 57-61 (Barrigar testimony). Moreover, there was also ample evidence that despite this guidance from the regulatory team, both Defendants oversaw direction to the sales force to do just what the regulatory team said was prohibited. Both Defendants attended a National Sales Meeting where sales reps gave a best practices presentation encouraging their colleagues to steer their discussions with doctors about Stratus toward the topic of drug delivery.[44] Defendant Fabian also did numerous "field rides" with individual sale representatives and sent them follow up emails encouraging them to describe Stratus as "an extension of medical management / a delivery system."[45] In sum, contrary to Defendants' claim, there was ample evidence from

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[43] See GX1172 at ACC-002-0000553 (Cogan's 2009 National Sales Meeting slides); GX1168 at 1, 30-31 (Attorney Howard Holstein slides advising not to "solicit or prompt customer questions regarding off label uses").

[44] See GX1166 at 10 ("Keys To Success. Research Probes. What is your post-procedure medical management treatment strategy? Do you think a slowly, consistent, alluding [*sic*], absorbing distribution of a chosen solution for 14-28 days would be beneficial?"); 10 Trial Tr. 109-113 (Logan: probing questions in the Stratus presentation (GX1166) at 2009 National Sales Meeting referred to Kenalog and Nasacort).

[45] See GX1538 (Fabian email to sales rep following field ride). Contrary to the compliance presentations he was provided, Defendant Fabian told his sales representatives to prompt customer questions about the use of Stratus as a drug delivery device, giving them samples of questions to use, such as "What is your current medical management protocol[?] [W]hat patient would Stratus not be indicated for, if there is inflammation is there value?" Id. As the sales representatives testified, these were references to the Stratus as a drug delivery device. 11 Trial Tr. 36-38 (Ader: references to medical management in Fabian ride-along email referred to Stratus as a drug delivery device); 11 Trial Tr. 71-73 (testimony of Norm Bilsbury as

which the jury could have concluded that Defendants were not, in fact, attempting to follow the advice of Acclarent's regulatory personnel. United States v. Ortiz, 966 F.2d 707, 711 (1st Cir. 1992) ("[I]t is for the jury to choose between varying interpretations of the evidence."). In any event, the issue in no way indicates that the statute or regulations violate due process.

IV. THERE WAS MORE THAN SUFFICIENT EVIDENCE FOR JURY TO FIND TEN SHIPMENTS ADULTERATED AND/OR MISBRANDED

Defendants' argument that the Government was required to prove external marketing statements to each hospital listed in the counts of conviction is without basis. No matter how many times Defendants attempt to recast it, the fact remains that the introduction of the Stratus into interstate commerce intended for drug delivery was the crime, not its promotion. Promotion was just some of the ample evidence of the product's intended use. Based on all the evidence presented that the sole intended use of the Stratus was drug delivery, and the absence of virtually any evidence showing that Acclarent ever intended the Stratus to be used as a spacer or with saline, it was reasonable for the jury to conclude that *every* distribution of Stratus was a crime, regardless of how it was ultimately used.[46]

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to same). See also GX1238, 1239, 1290, 1318, 1319, 1332, 1341, 1406, 1407, 1487, 1550 (emails from Fabian following up on "field rides" and encouraging sales representatives to prompt discussions of Stratus as an extension of medical management / delivery device). Defendant Fabian also attended and oversaw New Hire Training during the course of which new Acclarent sales representatives were told to describe the Stratus as a device that would provide "targeted medical therapy." See GX1364 at 34, 46, 48 (Convery Successful Selling PowerPoint); 9 Trial Tr. 110 (Convery: gave his "Keys to Territory Success" PowerPoint (GX1364) four to six times); GX1366, GX1366_001; GX1530_001 (agendas showing Fabian attended and presented to the same New Hire Trainings).

[46] Nor do the cases upon which Defendants rely provide otherwise. For example, the Court in Kordel v. United States did not hold that improper promotional statements must accompany the product in order to prove a misbranding claim. 335 U.S. 345 (1948). In Kordel, the Court held that labeling is not restricted to what is on or inside the package, but concludes that "[o]ne article or thing is accompanied by another when it supplements or explains it…[n]o

The evidence here was sufficient for the jury to find that all physicians who used the devices were trained with materials and messages about the unapproved use – including training slides and brochures that showed the device filled with the milky white Kenalog-40.[47] The evidence, including witness testimony, promotional and training materials, demonstrated that the Stratus was intended for drug delivery from the inception of its distribution and throughout its nationwide distribution. The evidence showed that Acclarent had a nationwide sales strategy to achieve that goal, and that the device had no other plausible use.[48] Wendy Oakes and all the

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physical attachment one to the other is necessary." Id. at 350. Kordel does not address the intended use concept at all, let alone even suggest that to sustain a conviction for distribution of an unapproved product, the jury must hear evidence of external marketing claims to the purchaser of the product. While the definition of labeling is relevant to a false and misleading labeling misbranding theory, it is not relevant to Defendants' convictions for failure to provide premarket notification and lack of PMA approval. United States. v. Articles of Drug for Veterinary Use also does not support Defendants' claim. As discussed above, the case indicates that materials not shown to have been used for external promotion were properly submitted to jury to determine intended use. 50 F.3d at 500.

[47] See 4 Trial Tr. 61-62 (Vanderkarr: used Evolve training materials with physicians); GX1140 (2009 sell sheet for ethmoid and frontal Stratus); GX664 (Levine Stratus video showing Stratus injected with Kenalog); GX706 at 7 (Stratus Product Introduction slides showing photo of Stratus with white milky fluid in reservoir); GX2424 (2008 sell sheet for ethmoid Stratus with white milky fluid in reservoir); GX849 (Harfe email answering question from Acclarent Regulatory VP Su Mien Chong and explaining that liquid in photo of Stratus appearing in various marketing materials was Kenalog).

[48] See 7 Trial Tr. 163 (Oakes: during the planning stages of Stratus' development, Kenalog had been selected as the drug it would be used with); Ex. 2550 at FACT0048824-26 (Notes of Facteau sales force call: "We …. also believe that there is opportunity for a pharmacological approach . . . in either case local drug delivery has a role"); GX959 (invitation to entire sales force for Facteau Stratus sales call); GX990 (9/30/08 email from Acclarent VP of R&D to Acclarent in house employees on day of Stratus launch: "Congratulations Team Condor: Acclarent has planted the flag for sustained local drug delivery for our ENT customers and their patients.") 9 Trial Tr. 70-71 (Convery: describing call with entire sales force (GX1059) and Dr. Brandeisky in which Convery and Dr. Brandeisky described Stratus as drug delivery / medical therapy device (GX1518) and no mention was made of benefits of Stratus as postop spacer with saline); GX1166 at 10 (1/22/09 Stratus Powerpoint presented at 2009 National Sales Meeting: "Keys To Success. Research Probes. What is your post-procedure medical

sales representatives testified (1) that they were taught to – and did – market the Stratus with the claim that it was designed for use with Kenalog-40 and that any other substance would elute very quickly,[49] (2) that they were trained to sell Stratus for drug delivery,[50] (3) that they were not given any training about the benefits of its use with saline or without any fluid at all,[51] (4) that

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management treatment strategy? Do you think a slowly, consistent, alluding [*sic*], absorbing distribution of a chosen solution for 14-28 days would be beneficial?"); 10 Trial Tr. 109-113 (Logan: probing questions in the Stratus presentation (GX1166) at 2009 National Sales Meeting referred to Kenalog and Nasacort); GX1140 (2009 sell sheet for ethmoid and frontal Stratus); GX2424 (2008 sell sheet for ethmoid Stratus); GX849 (email to Regulatory VP stating that liquid in sell sheet photo of Stratus was Kenalog).

[49] See supra nn. 4-6; see also (Krinsky: trained that holes were "specially sized" for Kenalog; saline ran out "quickly" – in "seconds"); 11 Trial Tr. 83 (Bilsbury: what he learned in training was consistent with what he heard in Jason Elmore's FESS by Numbers presentation, which was that the pores were designed for saline).

[50] See 5 Trial Tr. 51 (Vanderkarr: Received consistent direction to position Stratus as device for targeted treatment with Kenalog); 7 Trial Tr. 37 (Vanderkarr: Did not believe she could sell any Stratus for use with saline); GX 1364 at 34, 46, 48 (New Hire Training Slides given by Kevin Convery four-six times describing how to sell Stratus for steroid delivery, but not saline); 9 Trial Tr. 110-111 (Convery: gave GX1364 four to six times); 8 Trial Tr. 203 (Convery: Acclarent R&D team described Stratus as a drug delivery device to doctors before commercial launch); 9 Trial Tr. 17 (Convery: Acclarent higher-ups described Stratus as a drug delivery device to doctors in 2008); 10 Trial Tr. 33-34 (Krinsky: Sales representatives were taught that Stratus' selling point was targeted delivery of Kenalog); 11 Trial Tr. 58-59 (Ader: Managers were "constantly" training representatives to sell Stratus for drug delivery); 11 Trial Tr. 83 (Bilsbury: Learned in training that Stratus was designed to elute Kenalog-40)."

[51] See 4 Trial Tr. 156 (Vanderkarr: she could not recall any pitches or talk tracks provided to recommend to a physician the use of the device as a spacer with saline"); 4 Trial Tr. 198 (Vanderkarr: never received any training or talk track on how to promote Stratus for FDA cleared use); 5 Trial Tr. 69 (Vanderkarr: never received training slides to show how to use Stratus as spacer with saline); 7 Trial Tr. 87-88 (Steffen: never received any training on – or any promotional material explaining – the benefit of Stratus as spacer with saline); 8 Trial Tr. 208 (Convery: never given any tools to promote Stratus for its cleared use as spacer with saline); 9 Trial Tr. 71 (Convery: could not recall any sales force meetings discussing benefits of Status as spacer with saline); 10 Trial Tr. 25-29 (Krinsky: was never trained on or told of any benefit of Stratus as a spacer with saline); 10 Trial Tr. 64-65 (Logan testimony that no one trained her on benefits of Stratus with saline or how to promote it for that use); 11 Trial Tr. 24-29 (Ader

they did not believe Stratus provided patients any benefit without a drug,[52] (5) that they never promoted it for its cleared use,[53] and (6) that they were unaware of any doctors using it with saline.[54] Doctor Armstrong testified that he learned at an Acclarent sponsored meeting for hundreds of physicians across the country, as well as at an Acclarent training, that the holes in the device were designed to elute Kenalog-40 in order to bathe the sinus over a period of time. 3 Trial Tr. 49, 66. The geographic diversity of the doctors and sales representatives is also evidence that could have persuaded a juror that training and direction on how to sell Stratus was company-wide, and that those practices reflected Stratus' intended use across the country.

The evidence demonstrated that the promotional brochures, product introduction slides, training slides and almost every other item to be shown to physicians concerning the Stratus

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testimony that he received no training on benefit of Stratus with saline and no sales tools, literature or videos that described the benefits of Stratus as spacer with saline).

[52] See 4 Trial Tr. 179, 198 (Vanderkarr never trained a doctor on using Stratus with saline because she "didn't see a benefit"); 7 Trial Tr. 37 (Vanderkarr did not believe she could sell any Stratus for use with saline); 7 Trial Tr. 87 (Steffen did not believe Stratus had any clinical benefit with saline or as a spacer); 10 Trial Tr. 28 (Krinsky did not believe Stratus provided patients any benefit when filled with saline and no doctor ever told him that it did); 10 Trial Tr. 66 (Logan believed that saline provided no benefit to the Stratus).

[53] See 5 Trial Tr. 125 (Vanderkarr testimony that she never sold Stratus for cleared intended use); 7 Trial Tr. 105-06 (Steffen did not know of any sales reps who successfully sold Stratus for cleared use and did not believe it was possible to do so); 8 Trial Tr. 208-09 (Convery never suggested to a physician that he/she use Stratus with saline); 10 Trial Tr. 66 (Logan testimony that she never recommended Stratus for its cleared use); 11 Trial Tr. 28 (Ader testimony that he never recommended Stratus for its cleared use).

[54] See 5 Trial Tr. 99 (Vanderkarr: she did not recall hearing that any physician had ever used Stratus with saline); 7 Trial Tr. 105-06 (Steffen: never saw or heard of any doctor using Stratus as spacer with saline); 9 Trial Tr. 58-59 (Convery: never saw Stratus used with saline in a live case); 10 Trial Tr. 31 (Krinsky: never saw or heard of any doctor using Stratus with saline); 10 Trial Tr. 66 (Logan: not aware of any doctor using Stratus as spacer with saline, never heard from other sales reps that doctors used Stratus for cleared use); 11 Trial Tr. 28-29 (Ader: never saw or heard of a physician filling Stratus with saline or using it just as a spacer).

contained a picture of the Stratus filled with Kenalog-40.[55] Since Kenalog-40 is white, milky substance, not clear like saline, this means that essentially all promotional brochures, presentations and trainings included a picture of the device for an unapproved use. Since there was also ample evidence that no physician was permitted to use the Stratus unless he or she went to an Acclarent training, the jury could have concluded that every physician who used the device was trained with materials portraying the Stratus filled with Kenalog-40.[56] It is hard to see how the jury could reach any other conclusion.

The Government also presented evidence from Massachusetts specifically. The jury heard from Barbara Logan, whose territory covered all of New England and upstate New York. Ms. Logan recounted the same training that her colleagues in other regions received: she was taught that Stratus was designed to elute Kenalog-40 and that saline would run out. 10 Trial Tr. 60-61. Like sales representatives around the country, she never promoted it for the on-label use and was never trained to do so. 10 Trial Tr. 64. She testified that she discussed Stratus' use with Kenalog "every day." 10 Trial Tr. 98. The evidence also included an email from Ms. Logan to doctors at Mass Eye and Ear that called Stratus "a reservoir for localized bathing of the ethmoid

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[55] See GX1140 (2009 sell sheet for ethmoid and frontal Stratus); GX664 (Levine Stratus video showing Stratus injected with Kenalog); GX706 at 7 (Stratus Product Introduction slides showing photo of Stratus with white milky fluid in reservoir); GX2424 (2008 sell sheet for ethmoid Stratus with white milky fluid in reservoir); GX849 (Harfe email answering question from Acclarent Regulatory VP Su Mien Chong and explaining that liquid in photo of Stratus appearing in various marketing materials was Kenalog); 4 Trial Tr. 61-62 (Vanderkarr: used Evolve training materials with physicians).

[56] See 4 Trial Tr. 31 (Armstrong: Acclarent required surgeons to attend company training before it would ship them the Stratus); 6 Trial Tr. 89 (Vanderkarr: Acclarent would not ship Stratus to a doctor who had not undergone training); 11 Trial Tr. 41 (Ader: Acclarent would not ship Stratus until a doctor attended training); 26 Trial Tr. 149 (Defense closing: Acclarent would not ship Stratus until the physician was trained).

cells, comprised of hundreds of precision formed micropores. . . for a temporary direct delivery of a fluid solution. . ." (GX2572). The email never mentioned the FDA cleared use. The jury also heard from Dr. Cathy Chong, who worked in the hospital associated with Counts 9, 15, and 17. Dr. Chong heard Ms. Logan's Stratus pitch, and recalled Stratus described as an implant with a reservoir that could elude medication slowly over time to help prevent polyp regrowth. 8 Trial Tr. 124. Moreover, defense witness Dr. Catalano, a member of Acclarent's advisory board from Massachusetts, admitted that he believed the saline was useless, that he never used the device without drug, and that he would never recommend it to another doctor for its cleared use as a spacer with saline. 24 Trial Tr. 41, 65-67. Based on all the evidence, a rational jury could have concluded that the 10 charged shipments were intended for drug delivery.

The fact that defense witness Dr. Hoisington from Iowa testified that he sometimes used the device with saline certainly does not suggest that this was the intended use of the Massachusetts shipments or that the jury's verdict was not supported. See Def. Mem. at 30.[57] The jury was also entitled not to believe Dr. Hoisington, who admitted that he had changed his story about how he used the Stratus from his first interview with government agents. 22 Trial Tr. 132-33. Even when there are conflicting accounts, resolution of such witness conflicts is a matter for the jury, not a basis for a Rule 29 acquittal. Ortiz, 966 F.2d 711.

[57] Dr. Hoisington also testified that he never began a surgery intending to use the Stratus with saline. Instead, he said that he only used it with saline if he discovered, after opening up a patient, that the patient's sinus was not diseased. 22 Trial Tr. 67. Then, he explained, despite having discovered that he did not need to operate on that sinus at all, he nonetheless left in the patient the Stratus, a foreign body, with saline. 22 Trial Tr. 62, 142. Thus, according to his own testimony, Dr. Hoisington's intended use was always to be with drug, unless he discovered after beginning the surgery that no treatment was necessary. The jury may just not have credited this nonsensical testimony.

V. THE CONVICTIONS FOR ADULTERATION AND MISBRANDING ARE NOT MUTUALLY EXCLUSIVE

Defendants' convictions for misbranding and adulteration are not mutually exclusive. Contrary to Defendants' argument, none of the facts supporting Defendants' adulteration convictions is inconsistent with – or "negates" (Def. Mem. at 36) – any fact necessary to convict Defendants of misbranding. To the contrary, as the jury necessarily found based upon the Court's instructions, Defendants' conduct caused the distribution of a device which both lacked required PMA approval and thus was adulterated, and for which Acclarent had not provided the required notice, and thus was misbranded.

These approval and notice requirements are not inconsistent, they are complementary. A manufacturer of a Class III device who fails to file for PMA approval or submit premarket notice violates both requirements. Filing a PMA application can satisfy the need for premarket notice to the FDA. See 21 CFR § 807.81(b) ("A premarket notification under this part is not required for a device for which a [PMA] application . . . is pending …."). In the absence of such a filing, however, a Class III device is both adulterated for lack of required PMA approval, 21 U.S.C. § 351(f)(1)(B), and misbranded, for lack of the required notice. 21 U.S.C. § 352(o) (providing that a device is misbranded "if a notice or other information respecting it was not provided as required by such section or section 510(k) [21 U.S.C. § 360(k)].").[58] There is nothing inconsistent about these requirements. See United States v. Higgins, 2011 WL 6088576, at *1, *14 (E.D. Pa. 2011) (recognizing defendant's guilty plea to introducing into commerce "adulterated ***and*** misbranded medical devices"; "In part these devices were misbranded …

[58] 21 CFR § 807.81(a) provides that a required premarket notification must be submitted at least 90 days before introducing a device into interstate commerce for the first time. Id.

because the FDA was not provided with timely premarket notification of a new intended use….The devices were adulterated because they were required to have, but did not have in effect an approved application for premarket approval . . .” (citing § 351(f) and § 352(o)); accord United States v. Huggins, 2011 WL 6180623, at *2 (E.D. Pa. 2011).

Defendants argue that, (1) had they filed a PMA application for the Stratus as a drug delivery device and (2) had that PMA application been pending, they would not have needed to file a premarket notification (a 510(k) as required by 21 U.S.C. § 360(k) and 21 CFR § 807.81). See Def. Mem. at 36. That is irrelevant because they did not file a PMA application. Defendants are incorrect, however, that notice under section 510k is not required if a PMA is required. If a PMA is pending, it provides such notice. If, as here, no PMA was filed, then there is an absence of notice, as well as lack of approval. Having failed to file a PMA application, Defendants caused the distribution of a device that was both adulterated under because it lacked a required PMA approval, and misbranded because it lacked the required no premarket notice.

VI. DEFENDANTS ARE NOT ENTITLED TO A NEW TRIAL.

Defendants fail to offer any basis for a new trial. Pursuant to Federal Rule of Criminal Procedure 33(a), the court may grant a defendant’s motion for new trial “if the interest of justice so requires.” Id. Such a remedy is to be used “only where there would be a miscarriage of justice and where the evidence preponderates heavily against the verdict.” United States v. Merlino, 592 F.3d at 32 (citation omitted). The court is permitted to weigh evidence and credibility; however, absent exceptional circumstances, the court should defer to the jury’s findings. United States v. Thrower, 746 F. Supp. 2d 303, 307 (D. Mass. 2010).

Motions for new trial based on allegations of prosecutorial misconduct must be assessed in light of whether individual incidents of misconduct “could have a cumulative impact on the

jury sufficient to affect the trial's outcome." United States v. Wihbey, 75 F.3d 761, 773 (1st Cir. 1996). The court must weigh whether allegations of prosecutorial misconduct in closing arguments "poisoned the well" badly enough to merit a new trial. United States v. Carpenter, 494 F.3d 13, 23 (1st Cir. 2007). Here, there was no such misconduct.

A. Evidence About the Stratus' Safety Was Not Improper or Unduly Inflammatory.

Defendants have argued that the Government "repeatedly asserted" that Stratus was dangerous, and that it elicited "graphic" testimony in order to inflame the jury. Def. Mem. at 39. However, the record shows that the Government merely explained to the jury what the procedure for implanting a Stratus entailed. Likewise, Dr. Armstrong's description of the trocar as a "spike" similar to a finishing nail, for example, was an accurate description of how the device is implanted with a trocar. Defense witness Dr. Catalano similarly described the trocar on direct examination as a "little metal spear" used to "pierce the bone."[59]

The Government also stated clearly from the beginning of trial that nobody died or went blind from using Stratus. 2 Trial Tr. 50. Any evidence about the risks or adverse events

[59] 24 Trial Tr. 11 (Catalano). Overall, it was Defendants who elicited the trial's most graphic testimony by asking witnesses about what might happen if doctors did not use Stratus and Acclarent's balloon products, and instead used another surgery, functional endoscopic sinus surgery (FESS). In opening, Defendants' counsel described FESS as a procedure "where they go in with a router. They go in with this straw-shaped device, with a rotating blade at the end, very sharp. Rotates 1,000 RPM, pops into the sinus and pulls out, sort of like a weed whacker, roto router, pulls out the tissue, the lining of the sinus, and it's permanent, permanent, painful. You get the picture." 2 Trial Tr. 121:1-6. Defendants elicited graphic descriptions of traditional FESS from witnesses, including describing it as bloody and painful, as requiring a lot of cutting and removal of bone and tissue, and as being "traumatic." 2 Trial Tr. 119, 121 (Defendants' Opening Statement); 6 Tr. 67, 75-76, 117, 180 (Vanderkarr testimony elicited by defendants); 9 Tr. 214 (Convery testimony elicited from Defendants); 22 Tr. 47, 54, 57 (Hoisington testimony elicited by Defendants). Defendants also cross examined Dr. Chong, about alternative procedures "breaking into the bone between the sinuses and the eye and the orbit, and causing vision changes or vision loss," and "cracking into the bone between the sinus and the brain and causing leakage of brain fluid, or even tearing the dura." 8 Trial Tr. 180.

associated with Stratus was used to explain how the device worked, to address the balancing process that doctors used when deciding whether the purported benefits of the Stratus outweighed the risks, and to prove that Acclarent salespeople, who claimed that all Acclarent's products, including the Stratus, were "proven safe and proven effective" did not give doctors all of the relevant information about the product and/or made false and/or misleading claims.[60] The Government was clear that it was not arguing that the device caused specific serious injuries – since the evidence of actual adverse events was in the nature of infections, and pain – but the adverse event evidence presented was highly relevant to the jury's assessment of whether the Acclarent's Stratus marketing claims were truthful and non-misleading.

The device at issue in this case was used in a surgical procedure in the head. A description of how that procedure was performed was simply relevant evidence. There were no bloody garments, graphic pictures of injured victims, or the other types of potentially emotionally moving evidence that have frequently been held to be nonetheless admissible. See United States v. Vazquez-Larrauri, 778 F.3d 276, 288 (1st Cir. 2015) (upholding admission of testimony describing one victim as bleeding out through a vein and another victim's head as "sort of squished by the shots;" photos of victim's body, and photos of the bloody crime scene); see also United States v. Ross, No. 15-1460, 2016 WL 4800800, at *4 (1st Cir. Sept. 14, 2016) (finding no abuse of discretion in admission of videos and images of child pornography even where defendant was willing to stipulate that his computers contained child pornography because

[60] See 5 Trial Tr. 66 (Vanderkarr: used slides for physician training that described all Acclarent's products as "proven safe, proven effective, proven patient friendly); 7 Trial Tr. 221 (Oakes: GX2558 shows poster at AAO booth describing Acclarent products as "proven safe"); GX1428 at ACC-044-0000739 (Elmore discussing Stratus with Kenalog: "the benefits to you as a surgeon are a safe and effective tool . . ."); GX2555 at 6-7 (describing Acclarent's products as safe, effective and patient friendly).

court "is not required to scrub the trial clean of all evidence that may have an emotional impact"). Defendants' claims of unfair prejudice are unfounded.

B. Defendants Are Not Entitled to a New Trial Simply Because the Government Did Not Immunize Debra Cogan.

Defendants are also not entitled to a new trial simply because the government did not immunize Debra Cogan. As discussed in the United States' opposition to Defendants' motion regarding Ms. Cogan, the United States is not required to immunize a witness. Dkt. 342, 5/9/16 Gov't Opp. to Defs' Mot. to Compel (citing Curtis v. Duval, 124 F.3d 1, 9-10 (1st Cir. 1997)). Moreover, the premise of Defendants' original motion, that the United States had selectively immunized one regulatory professional while keeping unavailable another is simply incorrect. In fact, none of the at least six regulatory and legal advisers involved in this matter (Holstein, Bellack, Yen, Fenandez, Su Mien Chong and Cogan) were called by either side. The fact that Su Mien Chong, Cogan's boss and the person who had direct interactions with the Defendants on these issues, was available to testify and Defendants chose not to call her demonstrates that Cogan's absence did not deprive the Defendants of the only source of evidence regarding (1) the regulatory department's views and (2) what was communicated to the Defendants on these topics. Furthermore, in light of the acquittal on the fraud counts, the testimony of regulatory personnel is of less relevance since good faith is not a defense to the counts of conviction.

VII. INCONSISTENT WITNESS TESTIMONY DOES NOT SHOW MISCONDUCT

Defendants now suggest that there was something improper about the United States asking witnesses questions about their memory of events, testimony which they argue was inconsistent with other evidence that Defendants prefer to credit, or even evidence they did not offer. Defendants are both incorrect that the testimony was in most instances inconsistent, and in any event, there was no misconduct.

The Government is not required to, and indeed cannot, insure that all witnesses recall all events in exactly the same way. As courts have found time and time again, conflicting or inconsistent testimony among witnesses does not amount to a due process violation that would require a new trial. See United States v. Doherty, 867 F.2d 47, 70 (1st Cir. 1989) (rejecting motion for new trial where defendants pointed out conflicting testimony from two government witnesses). As the Court explained in Doherty; "After reading the record, we can find no more than a conflict of testimony among witnesses. Neither Napue nor any other decision prohibits a prosecutor from calling witnesses who will present conflicting stories." See also United States v. Casas, 425 F.3d 23, 45 (1st Cir. 2005) (same and noting that "such conflicts are a matter to be explored on cross-examination and the credibility of each account is for the jury to determine.").

Nor does Napue v. Illinois, 360 U.S. 264, 266-67 n.2, 271 (1959) suggest to the contrary. Napue does not provide that merely eliciting inconsistent testimony is misconduct. In Napue, the key government witness testified, in response to the prosecutor's question, that he had not been promised any consideration in exchange for his testimony. The prosecutor knew that testimony was false because the prosecutor had told the witness that he would make "a recommendation for a reduction of his sentence." Moreover, the promise had not been disclosed to the defense, so the defense could not cross-examine the witness appropriately about it. Here, the information about which the Defendants complain was all the subject of extensive cross-examination and closing arguments. See United States v. Magana, 118 F.3d 1173, 1185-91 (7th Cir. 1997) (rejecting motion for new trial premised on alleged perjury by government witness where defendants cross-examined witness and argued in closing that witness's testimony was false); United States v. Kattar, 840 F.2d 118, 128 (1st Cir. 1988) (holding government's presentation of false testimony not prejudicial error where no reasonable likelihood it affected the verdict).

A. Questions About Knowledge of On-Label Use Were Entirely Proper.

Defendants complain that the United States elicited testimony from witnesses about their lack of knowledge of any on-label use of the Stratus, but knew that Dr. Hoisington had claimed that he used the Stratus with saline on some occasions.[61] Defendants introduced no evidence showing that these witnesses were in fact aware of any on-label use or testified untruthfully.

Dr. Hoisington, a defense witness and paid adviser to Acclarent, did testify previously and at trial that he used the Stratus with saline – but then later admitted at trial that he had told federal agents in the past that he used the Stratus with Kenalog. He was also shown on video describing the Stratus at the 2008 Sinus Forum as a "drug-delivery device" and describing its use with Kenalog.[62] Dr. Armstrong also testified, backed up by emails he wrote to Acclarent in 2008, that he saw Dr. Hoisington demonstrate the device with water or saline and it was clear, and Dr. Hoisington explained at the time, that it "did not hold water."[63] The jury was free to believe or disbelieve Dr. Hoisington's testimony that he on occasion used the device with saline. Other witnesses were properly questioned and testified as to their knowledge of on-label use. There is simply no inconsistency, and no misconduct.

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[61] See 5 Trial Tr. 99 (Vanderkarr only aware of physicians using Stratus with Kenalog); 7 Trial Tr. 105-106 (Steffen unaware of any physicians using Stratus with saline); 9 Trial Tr. 58 (Convery never saw Stratus used with saline in a live case); 10 Trial Tr. 31 (Krinsky never saw or heard of any physician using Stratus with saline); 10 Trial Tr. 66-67 (Logan unaware of any doctors using Stratus to deliver saline); 11 Trial Tr. 28-29 (Ader never saw or heard of any doctor use Stratus to deliver saline or as a spacer).

[62] See 3 Trial Tr. 49 (Armstrong testifies that Hoisington video demonstrated using Stratus with Kenalog); GX804 (Hoisington video shown at Sinus Forum 2008 in which he describes Stratus as a drug delivery device).

[63] See 3 Trial Tr. 61-63 (Armstrong testimony explaining that saline "squirted out" of Stratus and "did not inflate" and "therefore cannot work as labeled"); GX808 (Armstrong email to Acclarent explaining Stratus "does not hold water as advertised").

B. Potentially Inconsistent Memories of Convery and Steffen Do Not Establish Any Misconduct.

Defendants also argue that witness Kevin Convery testified that he removed the discussion of the Stratus for an unapproved use from his training slides prior to the April 2010 training attended by witness Benjamin Steffen. But that does not in any way indicate that the government knowingly elicited untrue testimony. Mr. Steffen testified that he recalled seeing the slides presented by Mr. Convery at his new hire training, including slides with specific mentions of recommendations for the use of Stratus for steroid delivery. Mr. Convery testified that he presented, GX1364 – a slide deck describing Stratus exclusively as a steroid delivery device that could provide targeted medical therapy – four to six times at New Hire trainings. 9 Trial Tr. 111. He was then asked, on cross-examination, whether he gave a different slide presentation that did not include a discussion of Stratus, DX2314, at an April 2010 New Hire Training. In response, he first testified that he could not remember specifically. 9 Trial Tr. 173. Despite that testimony, in response to a leading question from defense counsel, Mr. Convery later changed his testimony and agreed that "as far as [he] knew," he gave s modified version at the April 2010 training attended by Mr. Steffen. 9 Trial Tr. 176-77. Thus, Mr. Steffen was firm about what he saw at his training and Mr. Convery was, at best, equivocal. This is no indication of false testimony, let alone misconduct. United States v. Tavares, 93 F.3d 10, 14 (1st Cir. 1996) (defense's ability to point to inconsistencies in testimony of government witnesses did not show prosecutorial misconduct because "inconsistent testimony by itself does not amount to perjury").

Moreover, unlike the situation in Napue, where the defendant could not have known of the false testimony by the government witness, the supposed inconsistency between Mr. Convery's and Mr. Steffen's was well known to the Defendants at trial, addressed by them with

the witnesses and argue the point in their closing.[64] Doherty, 867 F.2d at 70. For this reason, as well, Defendants also cannot show any reasonable likelihood that any potential inconsistency affected the verdict.

C. Asking Whether A Defendant Was Present Is Not Misconduct.

Defendants claims of misconduct concerning questions to Mr. Barrigar are equally without merit. Mr. Barrigar was always clear that he was uncertain as to his memory. When asked about who participated in a steering committee presentation dated August 14, 2007, Mr. Barrigar testified that he did not recall who exactly was in the meeting. 12 Trial Tr. 21. He further testified he did not know for sure if it would include the head of sales. Id. When asked who was the head of sales at that time, he stated "I believe it was Pat Fabian at this point." Id. In fact, Mr. Fabian did not start at Acclarent until several days later. This misrecollection was promptly cleared up on cross-examination. 13 Trial Tr. 163-65. There was no misconduct and no prejudice.

D. Asking About How Acclarent Handled Trade Shows Is Not Improper.

Defendants' argument that the Government improperly elicited evidence about Acclarent's marketing of the Stratus for drug delivery at an Outside the U.S. ("OUS") booth at a trade show in the United States in order to show that such promotion "violated FDA rules" is also incorrect. The testimony of Wendy Oakes cited by Defendants was elicited to establish that

[64] See 9 Trial Tr. 173-177 (Convery: regarding training presentation); 26 Trial Tr. 161-165 (defense closing discussing Convery and Steffen testimony); Notably, the Government informed Defendants that they would be using the off-label Convery presentation, GX1364, with Mr. Steffen during his direct exam five days before Mr. Steffen testified. See Att. E, 6/9/16 Callahan Email to Defense Counsel. Despite having that information and despite having the April 2010 Convery presentation, DX2314, Defendants chose not to confront Mr. Steffen with it in their cross-examination of him. 7 Trial Tr. 128-154.

at this trade show, Acclarent did not discuss or demonstrate the utility of the Stratus as a spacer with saline to any healthcare practitioner, but did demonstrate and promote the Stratus to deliver drugs to anyone who expressed any interest in the product. Thus, the evidence was introduced to establish, not that it was improper to have an OUS booth, but to prove that domestic physicians were redirected to the OUS booth for a demonstration about an unapproved use, rather than instructed about the on-label use at the US booth.[65]

CONCLUSION

This Court carefully considered each of the issues raised in Defendants Motion for Acquittal prior to and at trial and carefully instructed the jury on each of these issues. Defendants and the Amici seek to revisit these issues, but the Court's rulings followed settled law. The Defendants are also incorrect in suggesting any inappropriate conduct by the Government here, let alone pointing to the kind of unaddressed misconduct that would be necessary to require a new trial. For all of these reasons, Defendants' Motion for Acquittal or New Trial should be denied.

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[65] Defendants' are also incorrect in their claim that the FDA has "long taken the position that promotion of devices for use outside the United States is permissible." See Def. Mem. at 48. As the government pointed out when Defendants proposed to offer such testimony or seek such an instruction, Defendants' own expert stated the opposite. In a 1997 article, Mr. Shapiro wrote: "if a device is cleared or approved in this country for one use, it cannot be displayed at trade shows for another use that is only approved abroad. To be displayed, the device must be completely unavailable for sale in the United States for any intended use." Shapiro, "Displaying Investigational and Unapproved Medical Devices According to FDA Policy." See Att. F. The government asked Defendants to (1) provide any public statements evidencing such a policy and (2) explain Mr. Shapiro's prior inconsistent position. Instead, Defendants thereafter chose not to call Mr. Shapiro (thereby avoiding cross-examination on this point) and did not further seek such an instruction, thereby waiving any possible issue.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF).

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