Nos. 21-1326 and 22-111

In the Supreme Court of the United States

UNITED STATES, EX REL. TRACY SCHUTTE, ET AL.,
PETITIONERS
v.
SUPERVALU INC., ET AL.

UNITED STATES, EX REL. THOMAS PROCTOR,
PETITIONER
v.
SAFEWAY, INC.

ON WRITS OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE SEVENTH CIRCUIT

BRIEF FOR ADVANCED MEDICAL TECHNOLOGY ASSOCIATION, BIOTECHNOLOGY INNOVATION ORGANIZATION, AND MEMBERS OF THE MEDICAL INFORMATION WORKING GROUP AS AMICI CURIAE IN SUPPORT OF RESPONDENTS

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INTEREST OF AMICI[1]

The Advanced Medical Technology Association (AdvaMed) is the world's largest medical-technology association representing device, diagnostics, and digital

[1] No counsel for any party authored this brief in whole or in part, and no person or entity, other than amici curiae or their counsel,

technology manufacturers that are transforming health care through earlier disease detection, less invasive medical procedures, and more effective treatments. Its more than 400 member companies span every field of medical science and range from cutting-edge startups to multinational manufacturers. AdvaMed's member companies are dedicated to advancing clinician and patient access to safe, effective medical technologies in accordance with the highest ethical standards.

The Biotechnology Innovation Organization (BIO) is the principal trade association representing the biotechnology industry in all fifty states and abroad. BIO has approximately 1,000 members, ranging from small start-up companies and biotechnology centers to research universities and Fortune 500 companies. The majority of BIO's members are small companies that have yet to bring products to market or attain profitability. Roughly 80% of BIO's corporate members have annual revenues of under $25 million. These members rely heavily on venture capital and other private investment.

The Medical Information Working Group (MIWG) is an informal working group of manufacturers of biopharmaceutical products and medical devices. MIWG was formed in 2006 to improve the regulatory framework and enforcement climate affecting manufacturers' dissemination of information about their products, including information about "off-label" uses of lawfully marketed products. MIWG and its members have made numerous submissions to the Food and Drug Administration (FDA), including petitions seeking clarification of,

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made a monetary contribution intended to fund the preparation or submission of this brief.

and substantive changes to, the existing regulatory framework governing manufacturer communications. Members of MIWG submitting this brief as amici curiae include Amgen Inc., Bayer Healthcare Pharmaceuticals, Inc., Eli Lilly and Company, GlaxoSmithKline, LLC, and Pfizer, Inc.

Amici's members operate in heavily regulated fields, and they seek in good faith to comply with all applicable federal and state laws. The regulatory scheme governing the healthcare and life sciences sectors is immensely complex, and regulatory standards in many areas are ambiguous. Petitioners and the government have argued that the government is not "lax about * * * resolving ambiguities" in the regulations by which amici's member companies must abide, Pet. 25, and that "a sophisticated business that plans to present a large number of claims * * * and also has open lines of communication with the Government and its agents—certainly should ask about doubtful questions before claiming public funds," Pet. Br. 37-38. In amici's experience, these arguments significantly overstate how readily, in practice, regulated parties can obtain clarity in these complex regulatory environments. More generally, amici's members are all too aware of how regulatory ambiguity, combined with the threat of potentially devastating damages and penalties if defendants are deemed to have violated the statute, can deter investment in, and the undertaking of, critical healthcare innovation, and even the sharing of scientific information that can save lives.

SUMMARY OF THE ARGUMENT

Biopharmaceutical and medical device manufacturers operate in a complex and highly regulated industry, governed by an intricate web of laws and regulations administered and enforced by myriad state and federal agencies. The complicated regulatory and enforcement scheme established by the Food, Drug and Cosmetic Act (FDCA) lies at the center of this labyrinthine landscape. Some of those regulations are notoriously ambiguous and subject to varied interpretations. Yet *qui tam* relators—and often the government itself—assert that alleged violation of one of these nebulous regulations promulgated under the FDCA gives rise to liability under the False Claims Act (FCA).

If, as petitioners contend, FCA liability, including treble damages and statutory penalties, can be established on the basis of a purported violation of an ambiguous regulation, even when the defendant was acting consistently with an objectively reasonable interpretation of that regulation, the prospect of such liability will deter a considerable amount of investment and innovation in healthcare, and even communication about new medical treatments. This Court's precedent emphasizes that such over-deterrence of matters regulated by FDA is inconsistent with Congressional intent and, in the case of medical information, contrary to First Amendment protections. Reaffirmation of the scienter standard articulated by this Court in *Safeco Insurance Co. of America* v. *Burr*, 551 U.S. 47 (2007), which has long been applied to the FCA in the majority of circuits, would protect against this over-deterrence in such highly regulated areas as medical devices, biologics, and pharmaceuticals.

1. Regulatory regimes in the life sciences context are notoriously complicated. The statutes, regulations, sub-regulatory guidance documents, and other informal pronouncements, which are often not fully consistent, make it difficult and sometimes impossible for even the most sophisticated companies to divine how a particular rule might apply to its specific facts.

a. Some FDCA regulatory regimes employ standards that are not easily susceptible to bright-line rules. Rather, application of these regulatory standards requires the exercise of judgment by the regulators weighing competing policy considerations, which makes clarity regarding the rule nearly impossible to achieve, until after the agency has made its final pronouncement.

This Court addressed one such regime in *Buckman Co.* v. *Plaintiffs' Legal Committee*, 531 U.S. 341 (2001). There the Court considered a state law fraud claim premised on the allegation that a particular medical device should have been classified as a so-called Class III device, subject to FDA's most stringent approval pathway, instead of as a Class II device, subject to less demanding standards. Under the "510(k) process," FDA may reclassify a device into Class II if it determines the device is "substantially equivalent" to an existing, predicate device. 21 U.S.C. 360c(f)(1)(A)-(B). In *Buckman*, this Court recognized that application of the 510(k) process requires FDA to balance numerous, sometimes competing, priorities in determining whether a device meets the 510(k) standard. 531 U.S. at 348-349. The Court noted that, for this reason, Congress forbade private enforcement of the FDCA (by individuals or states). See *id.* at 352. Yet at least one court of appeals has allowed a *qui tam* relator to pursue a "fraud-on-the-

FDA" action based on allegations, which FDA has never embraced, that the manufacturer had improperly invoked the 510(k) standard. See *Dan Abrams Co.* v. *Medtronic, Inc.*, 850 F. App'x 508 (9th Cir. 2021) (unpublished). That same court has allowed relators to pursue FCA claims based on alleged violations of Current Good Manufacturing Practices (CGMPs), even when the government had taken no action to remove the product from the market. See *United States ex rel. Campie* v. *Gilead Scis., Inc.*, 862 F.3d 890 (9th Cir. 2017), cert. denied, 139 S. Ct. 783 (2019).

b. FDA's regulatory scheme governing communications by manufacturers is another complex regime that is rife with undefined terms and ambiguities. The FDCA prohibits manufacturers from selling unapproved biopharmaceuticals and medical devices and deems "misbranded" any drug or device with labeling that lacks "adequate directions for [its intended] use." 21 U.S.C. 331, 352(f)(1). Relying on an overbroad regulatory definition of "intended use" despite First and Fifth Amendment concerns, FDA has asserted authority to treat truthful speech about "off-label" use of products as evidence of an "intended use" beyond the scope of FDA's approval or clearance, and thus evidence of criminal misbranding. FDA has simultaneously long recognized that off-label use of products is both lawful and sometimes even the standard of care. The agency has further acknowledged the important role that manufacturers have in disseminating truthful, non-misleading scientific information to support such use, as well as the importance of "scientific exchange" about, unapproved products and uses. Reflecting the impracticalities of this

reality, FDA's guidance includes so-called "safe harbors" that identify contexts in which pre-approval and off-label communications may be appropriate. However, these purported "safe harbors" are narrow, ill-defined, and fail to provide manufacturers certainty, as FDA has failed to codify most of them in formal regulations, and they therefore lack binding effect on the Department of Justice or other enforcement authorities.

Further, FDA has failed to promulgate clear and legally binding definitions of fundamental regulatory terms, including "advertising," "labeling," "scientific exchange," and "promotion," despite numerous requests from amici, leaving the line between prohibited and permitted speech undefined, unclear, and subject to change. Nearly all FDA regulations governing manufacturer communications are decades old, and the agency accomplishes the vast majority of its policymaking through non-binding guidance documents—many of which are in tension with Constitutional and statutory limitations or other FDA regulations or guidance documents, and most of which are never finalized.

The daunting task of attempting to predict how FDA will reconcile these ambiguous, even conflicting, regulatory and sub-regulatory pronouncements is, in many instances, impossible even for the most sophisticated manufacturers. For new entrants contemplating investment in new technologies, if the risk of a mistake in that prediction could lead to devastating liability, the decision will often be not to invest at all.

2. To avoid the risks and costs associated with defending an FCA suit predicated on the alleged violation of ambiguous regulations, relators and the government

contend that the answer is simply to ask the government to clarify the regulatory standard. But amici and their constituent members repeatedly have done just that, without success.

Amici have, for example, filed multiple citizen petitions and made dozens of other public submissions to FDA, entreating it to issue binding regulations reconciling inconsistencies and defining key terms, including some that are relevant to whether FDA has jurisdiction to regulate a particular communication. Many of these requests have fallen on deaf ears. In some instances, FDA has acknowledged the issues with which amici are concerned, but years later still has not issued any clarifications—or worse, the purported clarifications have only further obscured the issue.

In the absence of clear, binding, and coherent rules to guide manufacturer communications, amicus MIWG has repeatedly asked FDA to establish an advisory opinion process that would give manufacturers an opportunity to vet the legality of specific contemplated activities with FDA. Although this is precisely how the government proposes in this case that regulated entities should proceed, FDA has thus far declined to establish an advisory opinion process.

Moreover, petitioners' position erroneously presupposes that a relator's proposed resolution of a given ambiguity is the same resolution the responsible government agency would reach. In many cases, however, that is a dubious, or at least uncertain, proposition. In many instances, a regulatory ambiguity exists when a relator files a *qui tam* action. Even if a relator persuades a

judge and jury that the manufacturer's objectively reasonable interpretation was "wrong" and its claims for payment "false," there is at least some possibility that the agency itself would have taken a different view.

The risk that, in the context of an ambiguous standard, a jury could find a claim "false" even when the agency would not is particularly great when relators are allowed to pursue FCA suits based on regulatory interpretations that the regulator itself has never articulated. FCA suits predicated on asserted violations of CGMPs or of the medical device 510(k) process, when FDA has not acted to remove the product from the market or taken other regulatory or enforcement action, run a high risk that a manufacturer could be held liable notwithstanding that the government itself held the objectively reasonable interpretation under which the manufacturer's conduct permissibly proceeded. Indeed, in the context of a device that FDA cleared for marketing, the strongest evidence (at least until that clearance is withdrawn) is that FDA believes the device *was properly cleared*. In such circumstances, the manufacturer *has already* obtained the best indication of the agency's position on the regulatory question and should not be subject to potential FCA liability for acting consistent with that indication.

3. As this Court's free speech and Due Process jurisprudence reflects, clarity as to what the law prohibits is essential to avoid unfairness and chilling protected speech. The *Safeco* rule, which the majority of circuits have applied to the FCA for years, is consistent with those principles. Petitioners' proposed rule, on the other hand, is not.

A company's alleged non-compliance with the FDCA and the rules and regulations promulgated thereunder can, in some circumstances, be asserted as the predicate for "false claims" under the FCA. Accordingly, a manufacturer that conveys truthful, non-misleading, scientifically important information about its products despite acknowledged ambiguity in the regulatory framework and is later deemed to have violated that unclear law can face the threat of treble damages and even more in statutory penalties, plus potential exclusion from federal health insurance programs—a fate that courts have described as a corporate "death penalty." The natural consequence of this legal regime is that manufacturers will refrain from sharing information about their products that is necessary to inform healthcare decisions and is critical to patient care.

While ambiguity in FDA's regulatory framework governing manufacturer communications has a profound impact on all medical product manufacturers, challenges in this regard are particularly acute for smaller companies, including many members of amicus BIO. Emerging companies, which may have only a single marketed product or a few products in development, frequently lack the robust internal compliance infrastructure or resources necessary to devote to parsing these ambiguities. For these companies, a single FCA threat or regulatory enforcement action could be a death blow, resulting in an insurmountable financial liability. Such companies must, then, make the choice between censoring themselves to ensure that they are not running afoul of FDA's ambiguous regime at the risk of losing investment opportunities that could spur meaningful innovation, or taking the risk of sharing necessary information

without being able to fully assess the likelihood that the government will take potentially lethal action against the company.

These concerns are not merely hypothetical. Every year, the government collects billions of dollars in settlements from manufacturers who cannot risk litigating FCA suits to judgment, often for reasons independent of the merits of the case against them. Relators and the government have in the past brought and settled scores of FCA suits on the theory that "off-label promotion" gave rise to false claims for reimbursement. All the while, the government largely disregarded requests directly from industry participants for clarification on the rules of the road. Consequently, manufacturers have had no practical choice but to curtail speech that this Court has deemed to be of particular importance to the public health.

Reaffirmation by this Court of the rule it adopted in *Safeco* would protect against over-deterrence. By ensuring that companies can only be held liable for treble damages and statutory penalties when their conduct lacked an objectively reasonable grounding in the regulatory regime, manufacturers could invest, innovate, and communicate about their products with confidence.

ARGUMENT

I. THE REGULATORY LANDSCAPE IN WHICH PHARMACEUTICAL AND MEDICAL TECHNOLOGY COMPANIES OPERATE INVOLVES HIGHLY COMPLEX, OFTEN AMBIGUOUS REGULATIONS

Amici, manufacturers of biopharmaceutical products and medical devices, operate within a vast and intricate regulatory framework. Central to that regime is the FDCA, 21 U.S.C. 301 *et seq.*, which "grants the Food and Drug Administration * * * the authority to regulate, among other items, 'drugs' and 'devices,' " *FDA* v. *Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 120 (2000) (citing 21 U.S.C. 321(g)-(h), 393). The FDCA and its implementing regulations comprise an enforcement regime that has been recognized as both "complex" and "complicated." *Guy* v. *Travenol Lab'ys, Inc.*, 812 F.2d 911, 916 (4th Cir. 1987); *Nutrilab, Inc.* v. *Schweiker*, 713 F.2d 335, 336 (7th Cir. 1983).

Notwithstanding the recognized impenetrability of certain regulations promulgated under the FDCA or need for flexibility on FDA's part in applying regulatory standards, courts have often permitted private relators to pursue FCA suits in which "falsity" is premised on an alleged violation of ambiguous FDCA standards—even where the government's own actions seem to suggest otherwise. See, *e.g.*, *Dan Abrams Co.* v. *Medtronic Inc.*, 850 F. App'x 508, 511 (9th Cir. 2021) (mem.) (permitting a "fraud on FDA" case on the theory that the defendant's medical devices were allegedly inappropriate for the more streamlined 510(k) regime, notwithstanding that FDA had cleared the device and never removed it); *United States ex rel. Campie* v. *Gilead Scis., Inc.*, 862

F.3d 890 (9th Cir. 2017), cert. denied, 139 S. Ct. 783 (2019) (allowing FCA claim premised on alleged CGMP violations and improper laboratory conditions to proceed despite FDA's failure to take any action); Press Release, U.S. Dep't of Just., Par Pharmaceuticals Pleads Guilty and Agrees to Pay $45 Million to Resolve Civil and Criminal Allegations Related to Off-Label Marketing (Mar. 5, 2015), https://www.justice.gov/opa/pr/par-pharmaceuticals-pleads-guilty-and-agrees-pay-45-million-resolve-civil-and-criminal; Press Release, U.S. Dep't of Just., Allergan Agrees to Plead Guilty and Pay $600 Million to Resolve Allegations of Off-Label Promotion of Botox® (Sept. 1, 2010), https://www.justice.gov/opa/pr/allergan-agrees-plead-guilty-and-pay-600-million-resolve-allegations-label-promotion-botox.

A. The Regulation of Medical Devices Involves FDA's Exercise of Policy Judgments That Preclude Certainty Regarding Their Application

The web of statutes, regulations, and rules applicable to manufacturers of medical devices is particularly complicated. All medical devices used in the United States are regulated by FDA in a two-part process. First, a medical device is grouped into one of three classes depending on its risk profile. Second, the device's risk profile is used to determine what review process and controls are needed to provide a reasonable assurance of safety and effectiveness. See 21 U.S.C. 360c(a)(1)(A)-(C).

Devices first marketed after 1976 are presumptively Class III devices, but FDA may reclassify such a device into Class I or Class II if, for example, it determines the

device is "substantially equivalent" to an existing device in that classification. 21 U.S.C. 360c(f)(1)(A)-(B). The analysis of whether a device is "substantially equivalent" to another device is called the "510(k) process" after the relevant section in the FDCA. As this Court has recognized, the 510(k) process is a "comprehensive scheme" pursuant to which FDA must balance the key factors in determining whether a device is safe and effective for public use. See *Buckman Co.* v. *Plaintiffs' Legal Comm.*, 531 U.S. at 348-349. "[T]he § 510(k) process imposes upon applicants a variety of requirements that are designed to enable FDA to make its statutorily required judgment as to whether the device qualifies under this exception." *Ibid.* FDA's review process involves numerous, highly technical steps.

In addition to being complicated, this regulatory regime necessarily calls upon FDA to make policy judgments that only it can. As the Court explained in *Buckman*, FDA has "flexibility" under these provisions because it must "pursue[] difficult (and often competing) objectives," such as ensuring the safety of a device's on-label use, as well as the need for "competition" among devices, and not "delay[ing] health care professionals' ability to prescribe appropriate off-label uses." 531 U.S. at 349-351. The Court noted that, to avoid over-deterrence in conflict with FDA's policy choices, Congress had reserved enforcement of the FDCA to the United States and precluded it by individuals or states. See *id.* at 349 n.4, 352.

Yet at least one court of appeals has held that relators may pursue FCA suits alleging that a manufacturer's improper invocation of the 510(k) standard renders claims involving a cleared product "false," despite

FDA's clearance of the product and failure to withdraw that clearance. See *United States ex rel. Dan Abrams Co.* v. *Medtronic, Inc.*, No. LA CV15-01212, 2019 WL 12536543, at *3 (C.D. Cal. July 23, 2019), rev'd in part, 850 F. App'x 508 (9th Cir. 2021).

The CGMPs provide yet another example of relators pressing a view of a highly complex regulatory regime seemingly out of step with FDA's own views. The CGMPs are aimed at fostering quality procedures in drug manufacturing and preventing the production of unsafe or ineffective products. See 21 U.S.C. 371; 21 C.F.R. 210, 211. Assessing compliance with the interacting layers of CGMP regulation and FDA guidance requires unique expertise and judgment. Reflecting this nuance and complexity, FDA takes "Official Action" in only a small fraction of inspections, with far more being resolved through some "voluntary action" on the part of the manufacturer. See Food & Drug Admin., Data Dashboard, https://datadashboard.fda.gov/ora/cd/inspections.htm. Yet at least one court of appeals has held that CGMP violations render claims involving the product "false" under the FCA, even when the government did not take "official action" to remove the product. See *Campie*, 862 F.3d 890.

B. Manufacturers Are Frequently Subject to FCA Suits for Product Communications That Allegedly Violate Outdated, Incomplete, and Ambiguous Regulations

Another area of particular concern to amici is the regulatory scheme governing manufacturers' communications about their products. Most of the relevant regulations are decades old and comprise a regime replete

with ambiguities and inconsistencies. The FDCA and its implementing regulations generally prohibit manufacturers from promoting products that lack FDA approval or clearance, and FDA has asserted that truthful speech about the "off-label" use of approved or cleared medical products may constitute criminal misbranding. See *United States* v. *Caronia*, 703 F.3d 149, 161 (2d Cir. 2012). But at the same time, FDA has long recognized that off-label use is critical to patient care. See, *e.g.*, Food & Drug Admin., Draft Guidance for Industry Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices 2 (Dec. 2011) (recognizing that off-label use "may even constitute a medically recognized standard of care").

Recognizing the importance of off-label *prescribing*, FDA repeatedly has underscored the critical need for manufacturers to be able to share truthful, non-misleading, clinically relevant information. To that end, FDA has established various "safe harbors" identifying contexts in which communications about unapproved products and uses may be appropriate. However, these "safe harbors" are narrow and ill-defined, and because FDA has failed to codify them, they have no binding effect on the Justice Department or other enforcement bodies. FDA has also failed to promulgate formal definitions of terms that are fundamental to the regulatory regime, such as "scientific exchange" and "promotion," despite numerous requests from amici. See 21 C.F.R. 312.7 (proscribing "promotional claims of safety and effectiveness" of a drug before its approval, but permitting "the full exchange of scientific information * * * , including dissemination of scientific findings" regarding the product "in

development"). See, *e.g.*, Med. Info. Working Grp., Comments 28, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products, No. FDA-2016-N-1149 (Apr. 19, 2017) (urging FDA to "codify the definition of 'scientific exchange'" and "clarify pathways under existing law for manufacturers to engage in 'pipeline' communications with payors, institutional customers, and HCPs"). Because FDA has failed to act, the line between prohibited and permitted speech remains undefined, unclear, and subject to change.

In the absence of authoritative regulations, FDA accomplishes the bulk of its policymaking through nonbinding guidance documents—many of which are in tension with regulations or other guidance, and most of which are never finalized. See, *e.g.*, Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices, No. FDA-2011-D-0868 (Dec. 2011) (Draft Guidance, never finalized, on FDA's "current thinking about how [pharmaceutical and medical device] manufacturers can respond to unsolicited requests for information about unapproved or uncleared indications or conditions of use (off-label information) related to their FDA-approved or cleared products"); Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices - Revised Guidance, FDA-2008-D-0053 (Mar. 2014) (Draft Guidance, never finalized, on FDA's "current thinking on recommended practices for drug and medical device manufacturers * * * to follow when distributing to health care professionals or health care entities scientific or medical journal articles, scientific or medical refer-

ence texts, or clinical practice guidelines that discuss unapproved new uses for approved drugs or approved or cleared medical devices."). In fact, amici and other industry actors have, at various times, availed themselves of the notice-and-comment process to express concern that draft guidance documents exceed FDA's statutory authority or may be constitutionally deficient, and yet FDA may never finalize the guidance, which means the agency does not address stakeholder concerns, while the draft guidance remains in place, to be cited in enforcement actions.[2]

This Court has recognized the need "to ensure that ambiguity does not chill protected speech," *FCC* v. *Fox Television Stations, Inc.*, 567 U.S. 239, 254 (2012), which the current ambiguity, coupled with potential FCA liability does. But lack of clarity also impairs innovation.

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[2] The FDCA is not the only source of regulatory ambiguity for life sciences companies. Drug pricing regulation, at issue in the suits against respondents, is notoriously opaque. The Anti-Kickback Statute (AKS), 42 U.S.C. 1320a-7b, which is often a predicate for FCA liability, see 42 U.S.C. 1320a-7b(g), is another example. The government has construed the AKS's criminal prohibition against offering "remuneration (including any kickback, bribe, or rebate) * * * to induce" the purchase or recommendation of a federally reimbursed healthcare product or service, 42 U.S.C. 1320a-7b(b)(2), to encompass mere "influence," despite acknowledging that "to induce" in criminal statutes generally has a much narrower meaning. See generally Pfizer Amicus Br., *United States* v. *Hansen*, No. 22-179 (Jan. 25, 2023). The government has even applied the AKS to bar charities that cover copayments for all treatments for a given condition (thereby avoiding any risk of improperly steering prescribing decisions), notwithstanding prior contrary guidance. See *Pharmaceutical Coal. for Patient Access* v. *United States*, No. 22-cv-714 (E.D. Va. filed Nov. 9, 2022).

For startup companies with limited resources, regulatory uncertainty can pose substantial—even existential—risks. Uncertainty can lead to inefficient program design or market avoidance, both of which can harm innovation. While that is true, to some degree, of ambiguity in any regulatory regime, the problem is exacerbated when the risk of making a wrong prediction on how ambiguity will be resolved could have existential consequences under a statute such as the FCA.

II. The Challenges Amici And Others Have Faced In Obtaining Clarity From FDA Demonstrate The Limits Of Petitioners' Position

The government as amicus contends glibly that, to the extent regulatory ambiguities or overbreadth exist, they can be resolved by "seeking clarification when necessary." U.S. Br. 32. Amici's vast collective experience trying unsuccessfully to seek clarification from FDA belies this contention.

MIWG was formed for the explicit purpose of seeking clarity in FDA's regulatory scheme regarding the dissemination of truthful, non-misleading information about prescription drugs, biological products, and medical devices. To that end, for nearly 15 years, MIWG has engaged with the government numerous times, including by filing two citizen petitions and dozens of public submissions, to seek clarity on foundational questions bearing on its members' activities.[3] Among other re-

[3] All FDA submissions and amicus briefs filed on behalf of MIWG members are available at http://www.miwg.org.

quests, MIWG has asked FDA to issue binding regulations defining key terms such as "advertising," "labeling," and "scientific exchange," and to clarify inconsistencies in regulations, guidance documents, and Federal Register preambles (for example, to clarify that safe-harbored speech will not be used as evidence of intended use). See, *e.g.*, Med. Info. Working Grp., Comments, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products, FDA-2016-N-1149 (Apr. 19, 2017); Citizen Petition of Med. Info. Working Grp., FDA-2011-P-0512 (July 5, 2011); Citizen Petition of Med. Info. Working Grp., FDA-2013-P-1079 (Sept. 3, 2013); AdvaMed, Comments, Draft Guidance for Industry: Distributing Scientific and Medical Publications on Unapproved New Uses - Recommended Practices, FDA-2008-D-0053 (May 2, 2014). BIO and AdvaMed have likewise appealed to FDA for clarifications in these critical areas on multiple occasions. See BIO, Comments, Communications and Activities Related to Off Label Uses of Marketed Products and Use of Products Not Yet Legally Marketed, FDA-2011-n-0912 (Mar. 12, 2012); AdvaMed, Comments, Clarification of When Products Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding 'Intended Uses'; Further Delayed Effective Date; Request for Comments, FDA-2015-N-2002 (July 18, 2017) (encouraging FDA "to issue a policy or framework addressing manufacturer communications regarding unapproved uses of approved or cleared medical products that will safeguard appropriate manufacturer communications," including "much-needed clarification regarding the types of manufacturer communications and activities

that constitute protected 'scientific exchange' "); AdvaMed, Comments, Draft Guidance for Industry on Responding to Unsolicited Requests for Off-Label Information and Prescription Drugs and Medical Devices, FDA-2011-D-0868 (Mar. 29, 2012); AdvaMed, Comments, Communications and Activities Related to Off-Label Uses of Marketed Products and Use of Products not Yet Legally Marketed; Request for Information and Comments, FDA-2011-N-0912 (Mar. 27, 2012). Yet most of these ambiguities remain unresolved.

In some instances, FDA has acknowledged ambiguities and "granted" stakeholders' requests for clarification, including in 2014 when FDA issued a partial grant of MIWG's citizen petitions by committing to engaging in a "comprehensive review" of rules and policies "for areas where it can refine and clarify the distinction between permissible and impermissible conduct." See, *e.g.*, Food & Drug Admin., Response Letter to Citizen Petition of the Medical Information Working Group 2, FDA-2011-P-0512 and FDA-2013-P-1079 (June 6, 2014) ("Petitions are granted to the extent that they seek greater regulatory clarity on the four specified topics [(1) manufacturer responses to unsolicited requests; (2) scientific exchange; (3) interactions with formulary committees, payors, and similar entities; and (4) dissemination of third-party clinical practice guidelines] and, more generally, that FDA engage in a comprehensive review of the regulatory regime governing communications about medical products."). But nearly nine years later, FDA has issued only one final guidance that is directly relevant to the commitments made in 2014 and has provided

no update on the status of the so-called "comprehensive review."[4]

Additionally, MIWG has repeatedly asked FDA to establish an advisory opinion process where manufacturers could vet proposed communications initiatives, but FDA has rejected MIWG's requests. See, *e.g.*, Med.

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[4] See Food & Drug Admin., Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers (June 12, 2018). With respect to the topic of manufacturer responses to unsolicited requests, FDA's draft guidance, issued in 2011 and never finalized, Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices, FDA-2011-D-0868 (Dec. 2011), was controversial and widely viewed by industry participants as impractical, untethered to prior FDA pronouncements, and inconsistent with Constitutional requirements. See, *e.g.*, Med. Info. Working Grp., Comments, Scientific Exchange, FDA-2011-N-091 and Responses to Unsolicited Requests, FDA-2011-D-0868 (Mar. 27, 2012); AdvaMed, Comments, Draft Guidance for Industry on Responding to Unsolicited Requests for Off-Label Information about Prescription Drugs and Medical Devices, FDA-2011-D-0868 (Mar. 29, 2012). While FDA also promised greater regulatory clarity regarding the definition of "scientific exchange," no guidance ever issued. FDA opened a docket on the topic in 2011 and many stakeholders filed comments, see FDA-2011-D-0868, yet FDA took no further action. Finally, while FDA issued draft guidance in 2014 on dissemination of clinical practice guidelines, see Food & Drug Admin., Draft Guidance for Industry: Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices (Feb. 2014), that too was widely criticized as too narrow, unworkable, and inconsistent with First and Fifth Amendment principles, see, *e.g.*, Med. Info. Working Grp., Comments, Draft Guidance for Industry: Distributing Scientific and Medical Publications on Unapproved New Uses - Recommended Practices, FDA-2008-D-0053 (May 2, 2014). As with many other guidance documents, FDA never finalized this guidance document or addressed stakeholder comments.

Info. Working Grp., Comments, Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products; Availability of Memorandum; Reopening of Comment Period 20-28, FDA–2016–N–1149 (urging FDA to adopt an advisory opinion process); *compare* Med. Info. Working Grp., Amended Comments, Food and Drug Administration Transparency Task Force FDA-2009-N-0247 (Apr. 15, 2010) ("[W]e respectfully request that FDA implement an advisory opinion process that would provide timely binding advice in response to a specific request on proposed promotional and scientific exchange practices.") *and* Dep't of Health & Human Servs., Transparency Task Force, FDA Transparency Initiative: Improving Transparency to Regulated Industry 44 (2011) (rejecting the request).

FDA has frequently rejected outright stakeholders' requests for clarification. When issuing its final Regulations Regarding "Intended Uses," 21 C.F.R. 201.128 (drugs); 801.4 (medical devices), for example, FDA explicitly denied numerous requests by MIWG and AdvaMed, among others, for clarifications on various aspects of the rule. *Compare* Med. Info. Working Grp., Comment 19, Regulation Regarding "Intended Uses," FDA-2015-N-2002-2049 (Oct. 23, 2020) (requesting clarification regarding the example of "repeated proactive detailing" in the preamble to the proposed rule because it was unclear and conflicted with prior agency statements), *with* Response to Comment 25, 86 Fed. Reg. 41,383, 41,396 (Aug. 2, 2021) (declining MIWG's request "because FDA does not believe the proposed clarification is warranted," including because FDA had issued non-binding guidance documents relevant to the in-

tended use determination); *compare* AdvaMed, Comments 4-5, Amendments to Regulations Regarding "Intended Uses'," FDA-2015-N-2002-2053 (Oct. 23, 2010) (noting that most of the examples FDA provided on a particular topic in the preamble were focused on the pharmaceutical industry and stating that "[a]dditional device-specific examples that would aid in representing the diversity of medical devices are needed") *and* Med. Info. Working Grp., Comments 20-24, Regulation Regarding "Intended Uses," FDA-2015-N-2002-2049 (Oct. 23, 2020) (identifying "inconsistent language in the preamble [that] creates the potential for confusion"), *with* 86 Fed. Reg. at 41,397 ("declin[ing] to make the requested modifications to the examples" and noting that "[e]ach scenario described in the preamble is fact-specific, and, under other circumstances or in other contexts, similar material may be evaluated differently").

In another instance, FDA has specifically acknowledged the non-binding nature of its guidance documents and solicited comments on whether such guidances should be codified, but has then, upon receipt of such comments expressing concerns about the lack of clarity, refused to consider them as "beyond the scope" of its rulemaking. *Compare* 85 Fed Reg. 59,718, fn. 7 (Sept. 23, 2020) (stating that FDA has issued various final guidance documents related to "safe harbors," and that "[t]he Agency has also recognized 'safe harbors' in draft guidance documents. When final, these documents will represent FDA's current thinking on these topics. The Agency invites comment on whether any elements of these guidances warrant codification in the regulations") (internal citations omitted), *with* 86 Fed. Reg. at 41,396 ("FDA welcomes and will continue to consider these

comments related to 'safe harbors.' However the recommendations made in these comments go beyond the scope of this rulemaking * * * . Expanding the scope of this rule to codify FDA's acknowledged 'safe harbors' or to acknowledge additional 'safe harbors,' as suggested in these comments, might warrant reproposing the rule to solicit additional input, unduly delaying the Agency's clarification of its regulations on intended use.").

The contention that companies need only ask the government for clarification if they are unsure about the applicable rules thus rings hollow.

The United States' blithe suggestion to ask the government for greater clarity also ignores that companies often have very good reasons—based on their dealings with the government—to feel confident that they are acting lawfully only to have that certainty called into question in a subsequent FCA lawsuit. As this Court has observed, Congress specified that the FDCA's provisions "be enforced exclusively by the Federal Government." *Buckman*, 531 U.S. at 352 (citing 21 U.S.C. 337(a)).[5] To that end, FDA keeps a close watch on the conduct of biopharmaceutical and medical device manufacturers in a variety of ways, including through routine surveillance and monitoring efforts, inspections, and

[5] In the FDCA, Congress specified not only that actions to enforce the FDCA must be brought "in the name of the United States," but also that they must be brought "*by* * * * the United States." 21 U.S.C. 337(a) (emphasis added). While a *qui tam* suit is brought in the name of the United States, this Court has recognized that an unintervened *qui tam* is not brought "by" the United States, "because the United States is not a party to an FCA action absent formal intervention or other meaningful participation." *United States ex rel. Eisenstein* v. *City of New York*, 556 U.S. 928, 931 (2009).

evaluation of complaints submitted by health care professionals and patients. The FDCA's regulatory framework affords FDA significant flexibility and discretion to carry out its mandate, and FDA "has at its disposal a variety of enforcement options that allow it to make a measured response to suspected fraud upon the Administration," including "by seeking injunctive relief, 21 U.S.C. 332, and civil penalties, 21 U.S.C. 333(f)(1)(A); seizing the product, 21 U.S.C. 334(a)(2)(D); and pursuing criminal prosecutions, 21 U.S.C. 333(a)." 531 U.S. at 349.

Notwithstanding FDA's exclusive authority to enforce the FDCA and its wide variety of remedial options for companies that err, courts have in some instances permitted FCA suits to proceed against defendants that had compelling reasons to believe that they understood what the law required of them, and that FDA did not view the company's behavior as out of step with those requirements. See, *e.g.*, *Dan Abrams*, 850 F. App'x at 511 (permitting a "fraud-on-the-FDA" case to advance to trial on the theory that the defendant's medical devices were allegedly only susceptible to uses that should have been subjected to the more rigorous PMA review process rather than the more streamlined 510(k) regime, notwithstanding that FDA had never withdrawn the clearance of the device).

The same has happened in the context of the CGMP provisions. In *Campie*, a relator was allowed to proceed on an FCA claim premised on alleged drug impurities supposedly introduced by CGMP violations and improper laboratory conditions, though FDA had taken no steps to remove the impacted drug from the market. 862 F.3d at 890.

By incentivizing plaintiffs to adopt interpretations of nuanced regulations grounded in the FDCA that may be different from the interpretations held by FDA, petitioners' proposed rule here would, in effect, empower lay juries to substitute their own speculation for FDA's actual assessments, even where the defendant has reason to believe, based on the agency's conduct, that the agency does not believe any wrongdoing was committed.

III. Adopting A Scienter Standard That Penalizes Actions Consistent With An Objectively Reasonable Understanding Of Ambiguous Legal Obligations Would Stifle Innovation And Chill Protected Speech

Although there are compelling and obvious reasons why the government as a matter of prosecutorial discretion should never bring an FCA action when the applicable legal framework is ambiguous, there is little doubt that this happens frequently, and even less doubt that the government permits relators to maintain cases in the government's name notwithstanding ambiguous statutory and regulatory regimes. See Part I, *supra*. When ambiguity exists, the burden should be on the government to clarify any ambiguity before prosecuting or allowing a case to be prosecuted in its name.

This Court has often said that the government and its agencies' interpretations of statutes and regulations are entitled to substantial deference. *National Cable & Telecomms. Ass'n* v. *Brand X Internet Servs.*, 545 U.S. 967, 980 (2005) ("*Chevron* requires a federal court to accept the agency's construction of [an ambiguous] statute, even if the agency's reading differs from what the court believes is the best statutory interpretation."); *Thomas*

Jefferson Univ. v. *Shalala*, 512 U.S. 504, 512 (1994) ("We must give substantial deference to an agency's interpretation of its own regulations."). When the meaning of an ambiguous provision cannot be definitively resolved until the agency has made a final determination, it is impossible for the regulated party to "know" that its construction is wrong until that resolution has occurred. See Resp. Br. 35-37.

The government's obligation to resolve such ambiguity *before* enforcing a statute or regulation is especially strong in the context of criminal statutes, such as the FDCA and the Anti-Kickback Statute, frequently used as a basis for FCA actions. See, *e.g.*, *Yates* v. *United States*, 574 U.S. 528, 547-548 (2015); *Skilling* v. *United States*, 561 U.S. 358, 410-411 (2010). "The rule of lenity requires ambiguous criminal laws to be interpreted in favor of the defendants subjected to them." *United States* v. *Santos*, 553 U.S. 507, 514 (2008) (collecting cases). "This venerable rule not only vindicates the fundamental principle that no citizen should be held accountable for a violation of a statute whose commands are uncertain * * * . It also places the weight of inertia upon the party that can best induce Congress to speak more clearly and keep courts from making * * * law in Congress's stead." *Ibid.* This is particularly true when, as here, amici's members have struggled, often in vain, trying to convince the government to provide greater clarity, and sometimes have even thought that they had succeeded, only to have that clarity undermined in a subsequent FCA litigation brought by a relator. See Part II, *supra*. Here, as in the criminal context, "the tie must go to the defendant." *Santos*, 553 U.S. at 514; see *Fox*

Television, 567 U.S. at 253-254 (noting Due Process principle "that regulated parties should know what is required of them so they may act accordingly").

Although it is a critical question, even more is at stake in this case than just whether an objectively reasonable interpretation of an ambiguous legal authority forecloses liability in a FCA suit. As a practical matter, the Court's answer to that question will have a powerful impact on amici's members' ability to bring innovative life-saving medical devices and medicines to market, and to communicate freely with health care professionals who prescribe their products and patients who need them.

The Seventh Circuit's standard, rooted in this Court's *Safeco* decision, has been applied by the majority of circuits, some for decades, without problem. Petitioners' proposed expansion of FCA liability, would, by contrast, place amici's members in an untenable position. If they were to act or speak in an area of legal ambiguity—even in an area where the government itself had acknowledged that ambiguity—and were later deemed to have violated the law, they would face the imposition of "essentially punitive" treble damages and possibly even more in statutory penalties, see 31 U.S.C. 3729; *Vermont Agency of Nat. Res.* v. *United States ex rel. Stevens*, 529 U.S. 765, 784 (2000). In some cases, they also would face the threat of exclusion from federal health care programs, "the so-called 'death penalty'" for healthcare and life sciences companies. *Public Citizen* v. *U.S. Dep't of Health & Hum. Servs.*, 975 F. Supp. 2d 81, 112 (D.D.C. 2013). That is the opposite of the clarity that this Court requires in punitive statutes.

Because a company's subjective understanding is a fact question, to escape those potentially fatal penalties in litigation, a company choosing to defend itself on the merits would most often have to bear the considerable costs and burdens attendant to litigation at least through summary judgment. And to have any hope of mounting a successful defense, companies may often be pressured to offer proof of their attorneys' opinion as to the correct interpretation of the ambiguous regulation at issue—undercutting both the burden of proof and the sacrosanctity of the attorney-client privilege. See Resp. Br. 53-54. Practically, as a result, amici's members would be forced to avoid the risk altogether by adopting the most conservative interpretation of any ambiguous legal obligation, even when doing so would severely hinder their ability to innovate, and/or require them not to speak—and even when sharing truthful, non-misleading, and scientifically important information about their products might be vital to product development or to patient care. A perfect example of this Hobson's choice is the ambiguous concept of "scientific exchange," which the FDA has been largely silent on since opening a docket in the matter in 2011. See 76 Fed. Reg. 81,508 (Dec. 28, 2011) (announcing the establishment of a docket and seeking "comments and information related to scientific exchange"). See Part II, *supra*. As technology advances, and the ways physician engage with information expands far beyond the analogue approaches previously considered, these problems will be exacerbated. While it may be objectively reasonable to assume some new digital means of information exchange should qualify for bona fide scientific exchange, manufacturers will remain chilled in advancing these innovations in the

event an agency (who has refused to clarify) simply disagrees post-hoc.

For emerging companies, this prospect raises the question whether the company will even get off the ground. As noted above, ambiguity in the field of what constitutes pre-approval communications frustrates manufacturers' ability to share truthful and non-misleading information about products in development and thereby to attract investors to fund further research and development efforts. For early-stage and emerging companies for whom investment is especially critical, the ability to engage in appropriate pre-approval communications can make the difference between success and failure. The risk of liability for acting consistent with an objectively reasonable interpretation of an ambiguous rule can mean that new medical treatments never come to market.

This Court noted Congress's concern for such over-deterrence in *Buckman*, when it expressed concern that "[w]ould-be applicants may be discouraged from seeking § 510(k) approval of devices with potentially beneficial off-label uses" due to fear of "unpredictable civil liability" for state "fraud-on-the-FDA claims." 531 U.S. at 350. The same concern exists if would-be applicants refrain from submitting applications for fear of unpredictable FCA liability if they are found to have guessed wrong about how a regulatory ambiguity will be resolved.

A scienter standard that fails to protect actions consistent with objectively reasonable interpretations of ambiguous legal obligations would also chill important,

constitutionally protected speech. This Court has affirmed that "[s]peech in aid of pharmaceutical marketing * * * is a form of expression protected by the Free Speech Clause of the First Amendment," and that any government restrictions on those communications are accordingly subject to "heightened judicial scrutiny." *Sorrell* v. *IMS Health*, 564 U.S. 552, 557 (2011). Indeed, the Court recognized in *Sorrell* that First Amendment protection for commercial speech is particularly important "in the fields of medicine and public health, where information can save lives." *Id.* at 566.

"Prolix laws chill speech for the same reason that vague laws chill speech: People 'of common intelligence must necessarily guess at [the law's] meaning and differ as to its application.' " *Citizens United* v. *Federal Election Comm'n*, 558 U.S. 310, 324 (2010) (quoting *Connally* v. *General Constr. Co.*, 269 U.S. 385, 391 (1926)) (brackets in original). It is for this reason that the Court must be wary of any rule, like the one advanced by petitioners here, that could impose liability—including for damages that "are essentially punitive in nature," *Stevens*, 529 U.S. at 784—based on a showing that a manufacturer had subjective reason to believe the government *might* view its conduct as unlawful based on its reading of an ambiguous regulation.

Amici's concerns are not merely hypothetical. Although the theory has become less prevalent in light of this Court's decision in *Sorrell* and the Second Circuit's holding in *Caronia* that truthful speech about off-label uses does not, by itself, violate the FDCA, companies have faced scores of FCA suits on the theory that defendants' off-label communications gave rise to false

claims for reimbursement. Relators and the government pursued these FCA suits notwithstanding the many ambiguities noted above afflicting FDA's pronouncements about manufacturers' product communications. Indeed, the government has collected billions in settlements from manufacturers who could not afford to risk litigating those cases to judgment. See, *e.g.*, Press Release, U.S. Dep't of Just., Shire PLC Subsidiaries to Pay $350 Million to Settle False Claims Act Allegations (Jan. 11, 2017), https://www.justice.gov/opa/pr/shire-plc-subsidiaries-pay-350-million-settle-false-claims-act-allegations (announcing settlement resolving allegations, *inter alia*, that defendants unlawfully marketed product for uses not approved by FDA); Press Release, U.S. Dep't of Just., Celgene Agrees to Pay $280 Million to Resolve Fraud Allegations Related to Promotion of Cancer Drugs For Uses Not Approved by FDA (July 24, 2015), https://www.justice.gov/usao-cdca/pr/celgene-agrees-pay-280-million-resolve-fraud-allegations-related-promotion-cancer-drugs.

If manufacturers can be held liable for speech that is consistent with an objectively reasonable interpretation of the regulations in question, many manufacturers will have no choice but to adopt the most conservative construction of those regulations, to avoid potentially punishing liability. That is a recipe for *maximizing* the chill on constitutionally protected speech, rather than *minimizing* it.

All of these adverse consequences would be avoided, however, if the Court would simply reaffirm the scienter standard it articulated many years ago in *Safeco*. Doing so would protect against the risk of over-deterrence that would inevitably stifle innovation and chill what this

Court has labeled "particularly important," lawfully-protected speech that "can save lives," by medical device, biologic, and pharmaceuticals manufacturers.

CONCLUSION

For the foregoing reasons, the judgments of the court of appeals should be affirmed.

Respectfully submitted.

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