

Testimony of Coleen Klasmeier on Behalf of the Medical Information Working Group
One-Page Summary

1. FDA's rules governing manufacturer communications are neither clear nor precise.

FDA has established four "safe harbor" policies recognizing the public health value of manufacturer dissemination of accurate information relating to off-label uses. Each safe harbor is subject to a number of vague qualifying criteria and burdensome additional requirements. The policies are also hard to follow because FDA has started but failed to complete proceedings to revise the safe harbor policies, and not all of the policies apply clearly to both drugs and medical devices. The lack of clarity corresponds to under-utilization of the safe harbors, which reduces clinically valuable manufacturer communication, undermines optimal patient care, and presents First and Fifth Amendment issues.

2. The existing FDA regulatory scheme for manufacturer communications is unstable.

FDA and the Department of Justice aggressively pursue enforcement actions with respect to "off-label" speech, but First Amendment arguments in those cases have been accepted by reviewing courts. Litigation has a destabilizing effect on the regulatory scheme and threatens FDA's ability to make incremental changes. The public health and legal consequences of the developing case law point up the need for modifications to the existing rules and policies.

3. Legislation could dramatically improve the regulatory scheme.

Legislation could be helpful in addressing FDA's seeming inability to make meaningful progress in reviewing and modifying the rules and policies governing manufacturer speech. Legislation could also stabilize the existing system in a more durable manner than regulations, which can be reversed through agency action or more easily invalidated through litigation. Legislation could also address the risk of a frontal assault on FDA regulation.

“Examining Medical Product Manufacturer Communications”
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Testimony of Coleen Klasmeier on Behalf of the Medical Information Working Group

Good morning. I am Coleen Klasmeier, a partner and head of the FDA regulatory practice at the law firm Sidley Austin in Washington, DC. I am appearing today on behalf of the Medical Information Working Group. The MIWG is an informal working group of manufacturers of biopharmaceutical products and medical devices, formed in 2006 to seek clarity in the enforcement and regulatory environment affecting communications about investigational and lawfully marketed medical products. Although we have been involved in a variety of efforts on these issues, from educational outreach to amicus briefs and submissions to federal agencies, the bulk of our work in recent years has involved FDA. We have made twenty submissions to FDA on manufacturer communications since 2008.¹ Today I would like to make three points.

1. FDA’s rules governing manufacturer communications are neither clear nor precise.

Decisions to prescribe and use lawfully marketed drugs and medical devices in ways that differ from the FDA-authorized labeling—“off-label use”—are a constituent part of medical and surgical practice, and can also be the standard of care.² FDA has long recognized the need for prescribers to receive, and manufacturers to have some ability to share, information outside of

¹ The MIWG’s submissions to FDA are available at www.miwg.org and www.regulations.gov.

² See, e.g., FDA Draft Guidance, Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices (Dec. 2011) (“FDA recognizes that these off-label uses or treatment regimens may be important therapeutic options and may even constitute a medically recognized standard of care.”).

product labeling to help support clinical decision-making.³ As a result, although a manufacturer is prohibited from “promoting” its product for “new uses,” it can lawfully provide information about off-label uses within defined circumstances. Currently there are four “safe harbors.” Only one is set forth in a binding regulation; the others are in non-binding documents.⁴ They therefore lack the force of law. Moreover, two of the four safe harbors have been the subject of ongoing FDA proceedings since 2011.

Under these policies, a manufacturer is ostensibly permitted to provide off-label use information without fear of enforcement in four sets of circumstances, involving (1) “scientific exchange,” (2) responses to unsolicited requests, (3) continuing education, and (4) reprints of certain journal articles, reference texts, and clinical practice guidelines. Each safe harbor is subject to a number of qualifying criteria and additional requirements which are unclear in many respects. Moreover, FDA has been unable to complete its process of revising the safe harbor policies, so questions frequently arise regarding the status of the old policies relative to

³ See, e.g., 59 Fed. Reg. 59,820, 59,822-23 (Nov. 18, 1994) (recognizing “the importance of dissemination of reliable scientific information on both approved and unapproved uses,” and describing “a number of policies” that permit manufacturer dissemination of information on “unapproved uses”); 37 Fed. Reg. 16,503, 16,504 (Aug. 15, 1972) (FDA “is charged with the responsibility for judging the safety and effectiveness of drugs and the truthfulness of their labeling. The physician is then responsible for making the final judgment as to which, if any, of the available drugs his patient will receive in the light of the information contained in their labeling and other adequate scientific data available to him.”) (emphasis added).

⁴ See 21 C.F.R. § 312.7 (scientific exchange, for drugs); 59 Fed. Reg. at 59,823 (unsolicited requests); 62 Fed. Reg. 64,093 (Dec. 3, 1997) (continuing education and similar activities); FDA Guidance, Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (Jan. 2009) (reprints).

the proposed new policies.⁵ In addition, there is a lack of symmetry between the policies for drugs and those for devices.⁶ In short, the safe harbors are a mess.

As a result, manufacturers cannot confidently rely on the safe harbors, and that has public health consequences. For example, it is common for the Advisory Committee on Immunization Practices—a statutory advisory committee to the CDC—to make recommendations for vaccines that are arguably “off-label.”⁷ An ACIP recommendation might vary the dosing frequency for a vaccine, for example. Under FDA rules, the vaccine manufacturer would be prohibited from promoting the vaccine in accordance with the ACIP recommendation. Moreover, its ability to engage in non-promotional, “safe harbored” communications about the ACIP recommendation would be significantly frustrated by the lack of clarity in the safe harbors, and in particular, the fear that communicating about the ACIP recommendation could be characterized by the government as unlawful off-label promotion. Ultimately, the public health benefits of the ACIP recommendation would not be advanced fully

⁵ For example, in December 2011, FDA launched a process to revise the “scientific exchange” and “unsolicited requests” safe harbor policies. The status of these efforts remains unclear. See 76 Fed. Reg. 81,508 (Dec. 28, 2011); 76 Fed. Reg. 82,303 (Dec. 30, 2011). FDA published a revised draft guidance on reprints, but the draft has not been finalized. FDA Guidance, Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices (Revised Draft Guidance) (Feb. 2014). In June 2014, FDA granted two citizen petitions filed by the MIWG, stating that the agency planned to issue guidance addressing “distributing scientific and medical information on unapproved new uses . . . and manufacturer discussions regarding scientific information more generally, by the end of the calendar year.” Letter from Leslie Kux, Assistant Commissioner for Policy, FDA to MIWG Counsel, Docket Nos. FDA-2011-P-0512 and FDA-2013-P-1079 (June 6, 2014).

⁶ For drugs, the “scientific exchange” safe harbor is codified at 21 C.F.R. § 312.7. The analogous regulation for medical devices, 21 C.F.R. § 812.7, omits the safe harbor language.

⁷ See, e.g., Morbidity and Mortality Weekly Report 2013; 62(RR04);1-34, available at https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm?s_cid=rr6204a1_w (recommending MMR vaccination for infants aged \geq 6 months who plan to travel or live abroad).

because the intended audience for the recommendation would not receive manufacturer communications reinforcing the advisory committee’s findings or advice.

The regulatory scheme likewise has legal consequences. The First Amendment case law makes clear that FDA is limited in its power to prohibit drug and medical device manufacturers from communicating about their products. The familiar Central Hudson test for commercial speech holds that accurate speech about lawful activity—and off-label use is, with very limited exceptions, lawful activity—is subject to constitutional protection.⁸ That means the government, in defending regulations that burden that speech, must demonstrate that those regulations are premised on a substantial government interest.⁹ In addition, the government must prove that its regulations directly advance that interest, and that the regulations are sufficiently tailored to the interest.¹⁰ More recently, the Supreme Court used a “heightened” scrutiny test in a case involving a state law restricting accurate manufacturer speech about prescription drugs, suggesting that the Central Hudson test for evaluating commercial speech regulation might not be protective enough of the speech.¹¹ The constitutional test for government regulation of scientific speech,¹² or “mixed” speech (communication that

⁸ Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm’n, 447 U.S. 557 (1980).

⁹ Id. at 564 (“The State must assert a substantial interest to be achieved by restrictions on commercial speech.”).

¹⁰ Id. (“First, the restriction must directly advance the state interest involved; the regulation may not be sustained if it provides only ineffective or remote support for the government’s purpose. Second, if the governmental interest could be served as well by a more limited restriction on commercial speech, the excessive restrictions cannot survive.”).

¹¹ Sorrell v. IMS Health Inc., 564 U.S. 552, 565 (2011).

¹² Miller v. California, 413 U.S. 15, 34 (1973); Keyishian v. Bd. of Regents, 385 U.S. 589, 603 (1967); Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51, 62 (D.D.C. 1998); Bd. of Trs. v. Sullivan, 773 F. Supp. 472, 474 (D.D.C. 1991).

inextricably combines scientific and commercial speech), is the even more demanding “strict scrutiny” test, and FDA regulations affecting those two species of communication would almost certainly be invalidated by a court.¹³

FDA’s regulatory scheme also implicates the Due Process Clause of the Fifth Amendment, which requires government agencies to establish clear rules that give fair notice of what is prohibited.¹⁴ The adoption of clear, binding rules is essential to bring FDA’s regulatory scheme into alignment with the Fifth Amendment.

2. The existing FDA regulatory scheme for manufacturer communications is unstable.

The lack of clear rules that allow manufacturers an appropriate measure of latitude to provide accurate information about their products is only part of the problem. FDA—and in important respects the Department of Justice, which represents FDA in court and brings its own investigations under the Federal Food, Drug, and Cosmetic Act, the False Claims Act, and other statutes—imposes aggressive restraints on manufacturer speech. Although manufacturers have settled many cases involving “off-label promotion” allegations in recent years, in some instances individuals and firms have raised First Amendment arguments in court, and those arguments have succeeded.¹⁵ Arguably the most famous example involves the Caronia case,

¹³ Riley v. Nat’l Fed., 487 U.S. 781, 796 (1988) (“Thus, where, as here, the component parts of a single speech are inextricably intertwined, we cannot parcel out the speech, applying one test to one phrase and another test to another phrase. Such an endeavor would be both artificial and impractical. Therefore, we apply our test for fully protected expression.”).

¹⁴ FCC v. Fox Television Stations, Inc., 132 S. Ct. 2307, 2318 (2012) (quoting United States v. Williams, 553 U.S. 285, 304 (2008)).

¹⁵ But see United States v. Harkonen, 510 F. App’x 633 (9th Cir. 2013), cert. denied, 134 S. Ct. 824 (2014).

invalidating a conspiracy conviction on First Amendment grounds.¹⁶ The Amarin case involved a manufacturer's assertion that its product could be marketed with out-of-label efficacy claims that FDA had found accurate but nevertheless sought to prohibit.¹⁷ In Pacira, FDA had granted approval for a prescription analgesic drug but later sought to prohibit the company from promoting the product according to its labeled indication.¹⁸ This string of decisions has led some observers to decry judicial involvement in adjudicating drug efficacy claims.¹⁹ In some cases, observers have gone further, claiming that the First Amendment case law is "incompatible with regulating drug promotion."²⁰

But maintaining the status quo ignores the law and harms the public health. FDA's regulatory scheme is at risk from additional lawsuits because, despite some incremental improvements, the rules continue to burden constitutionally protected speech. Keeping things as they are also ignores the Fifth Amendment requirements for clear, prospectively defined rules. The First and Fifth Amendments represent the principle that the public health is advanced by more, rather than less, accurate information to inform clinical decision making. Observers who seek to set the Constitution on a collision course with their own ideas about

¹⁶ United States v. Caronia, 703 F.3d 149 (2d Cir. 2012).

¹⁷ Amarin Pharma, Inc. v. FDA, 119 F. Supp. 3d 196 (S.D.N.Y. 2015).

¹⁸ Stipulation and Order at 2, Pacira Pharms., Inc. v. FDA, No. 15-7055 (S.D.N.Y. Dec. 14, 2015), ECF No. 45.

¹⁹ Joshua M. Sharfstein & Alta Charo, The Promotion of Medical Products in the 21st Century: Off-label Marketing and First Amendment Concerns, JAMA (published online Sept. 14, 2015).

²⁰ Aaron S. Kesselheim, Michelle M. Mello, and Jerry Avorn, FDA Regulation of Off-Label Drug Promotion Under Attack, 309 JAMA 445 (2013).

public health policy ignore the idea that free speech itself protects and promotes the public health.

To be clear, the MIWG does not support any reform measure that would take FDA out of its current role in reviewing claims of drug and device effect in advance. The measures we have requested involve targeted clarifications to the safe harbors and key statutory terms such as “labeling” and “intended use.” The MIWG has not sought dramatic changes to the regulatory scheme that would open the floodgates to off-label promotion. We have not asked for, and do not want, a health care system in which manufacturers can market their drugs and medical devices based on spurious or unsubstantiated claims of clinical utility. We have asked, instead, for clear rules that distinguish permitted from prohibited communications, and that provide manufacturers with reasonable latitude to communicate about their products.

3. Legislation could dramatically improve the regulatory scheme.

Although the MIWG has been dedicated to direct engagement with FDA on manufacturer communication issues, we recognize the paramount role of Congress and we believe that legislation may be necessary, for several reasons.

FDA action has been slow and ineffectual. It has been almost six years, for example, since FDA published a notice in the Federal Register soliciting public comment on the scope of the scientific exchange safe harbor and on a new draft guidance on unsolicited requests.²¹ Where FDA has taken action, the policy has tacked in the wrong direction, becoming less clear

²¹ See 76 Fed. Reg. 81,508 (Dec. 28, 2011); 76 Fed. Reg. 82,303 (Dec. 30, 2011).

and more speech restrictive.²² It appears FDA has been hamstrung by differing views internally and with the Department of Health and Human Services.²³ FDA officials might also be reluctant to do or say anything publicly that they believe would help tee up more litigation that they might not win.

For these reasons, it would be helpful for Congress to step in and set the overall policy and direction for FDA to implement. We believe that Section 3037 of the 21st Century Cures legislation, the so-called FDAMA 114 fix—is a paradigmatic example. There, Congress established a clear rule, and FDA promptly executed that rule through a reasonably clear and speech-enabling guidance document.²⁴

Legislation is more durable than unilateral FDA action. Statutory law is not subject to the same variability as agency pronouncements, and cannot be undone by agency leadership in a future Administration. Legislation would also be less susceptible to legal challenge than a regulation or a guidance document. Regulations have the force of law, but the Administrative Procedure Act creates a vehicle for challenge, whereas a statutory change could only be challenged successfully on constitutional grounds.

²² The new draft guidance on unsolicited requests includes six pages of criteria for determining whether speech qualifies for the safe harbor. The earlier iteration of the policy, published in 1994, comprised a single paragraph.

²³ Sources: FDA, HHS Leaders Clash On Off-Label Communication Next Steps, Inside Health Policy (Jan. 22, 2016), available at <https://insidehealthpolicy.com/daily-news/sources-fda-hhs-leaders-clash-label-communication-next-steps>.

²⁴ The amended provision is codified at 21 U.S.C. § 352(a). See FDA Guidance, Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities—Questions and Answers (Draft) (Jan. 2017), available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537347.pdf>.

Legislation may be necessary given the likelihood of continued judicial involvement.

Although we value the contributions that recent judicial decisions have made to the body of relevant constitutional and regulatory law, we also believe that litigation is not the ideal method of making law on issues that leave little room for error. We are particularly concerned by the possibility of a broadside attack on the FDA regulatory scheme that could result in the entry of a judicial order with significant and far-reaching consequences for the entire regulatory framework, including the agency's ability to enforce premarket review requirements.

We greatly appreciate the opportunity that this subcommittee had created for discussion of these important issues today. Thank you once again, and I look forward to your questions.