Journal of Law and the Biosciences, 192–195
doi:10.1093/jlb/lsw007
Advance Access Publication 23 February 2016
Response

# Affirming the need for a new model for the regulation of drug promotion: a rebuttal to Krause and Zettler

Alan Bennett[1,†], Freddy Jiménez[2,*,‡] and Larry Fields[3,**]

1. Ropes & Gray's, Washington, DC, USA
2. Law and Compliance, Celldex Therapeutics, Hampton, NJ, USA
3. Clinical Development, Janssen Pharmaceuticals, Inc, NJ, USA
*Corresponding author. E-mail: freddyjimenezesq@gmail.com

At the outset, we wish to thank Joan H. Krause[1] and Patricia J. Zettler[2] for their thoughtful commentaries on our article, 'Back to First Principles: A New Model for the Regulation of Drug Promotion'. Our New Model is intended as an 'initial' proposal for a modern, sustainable regulatory framework that comprehensively addresses drug promotion while protecting the public health, aligning FDA's policies with the First Amendment, establishing clear and understandable rules, and maintaining the integrity of the FDA approval process, so we appreciate the feedback and constructive criticism provided by the commenters. However, we contend that both commenters downplayed the impact of the First Amendment in establishing the urgent need for an overhaul of FDA's oversight of drug promotion.

Recent case law, including the Second Circuit's decision in *United States v. Caronia*,[3] has recognized that the First Amendment does not permit the government to prosecute truthful and non-misleading speech by drug manufacturers. Judicial developments since the publication of our article have continued to recognize the legality of such speech by drug manufacturers.

† Alan Bennett is a Life Sciences senior counsel in Ropes & Gray's Washington office.
‡ Freddy Jiménez is Vice-President, Law and Compliance, Celldex Therapeutics, Hampton, NJ.
** Larry Fields is Senior Director, Clinical Development, Janssen Pharmaceuticals, Inc.
1 Joan H. Krause, *Off-Label Drug Promotion and the Ephemeral Line Between Marketing and Education*, J. L. & Biosci. (last accessed Nov 18, 2015).
2 Patricia J. Zettler, *Regulating Drug Promotion to Promote the Public Health: a Response to Bennett et al.*, J. L. & Biosci. (last accessed Nov 5, 2015).
3 703 F.3d 149 (2d Cir. 2012).

First, in August 2015 in *Amarin Pharma, Inc. v. FDA*, a federal district court in New York granted a drug manufacturer preliminary injunctive relief to engage in truthful and non-misleading speech regarding the use of its triglyceride-lowering drug in a subpopulation that FDA had not approved.[4] The district court ruled that the manufacturer may make certain truthful statements about the potential benefits of its drug for patients with 'persistently high triglycerides', even though the drug lacks FDA approval for that particular use.[5] Relying on *Caronia*, the district court determined that the manufacturer's proposed off-label speech was constitutionally protected and could not, on its own, form the basis of a misbranding charge.[6] Although the government asserted that the *Caronia* decision should be limited to its specific facts, the district court disagreed and found that the *Caronia* holding was 'categorical, rather than case-specific'.[7] Moreover, the district court explicitly recognized—as did our original article[8]—that even though the FDA's regulatory framework was originally created in 1962, it must be considered and construed 'in light of contemporary First Amendment law, under which truthful and non-misleading commercial speech is constitutionally protected'.[9]

Second, in *Pacira Pharmaceuticals, Inc. v. FDA*, another drug manufacturer filed a lawsuit alleging that FDA violated the First and Fifth Amendments and the Administrative Procedure Act when it issued a warning letter that accused the manufacturer of off-label promotion.[10] The manufacturer alleged the challenged speech was 'on-label', rather than off-label, and even if it were off-label, it was truthful and non-misleading and therefore constitutionally protected.[11] Rather than litigate the case, the government reached a settlement with the manufacturer in December 2015. As part of the settlement, FDA took the unprecedented step of rescinding the warning letter issued to the manufacturer and revising the approved labeling of the manufacturer's drug to eliminate any ambiguity regarding its approved indications.[12]

The *Caronia*, *Amarin*, and *Pacira* cases have resulted in an urgent need to address the First Amendment problems created by FDA's restrictions on speech. The decisions in *Caronia* and *Amarin* both support the principle that truthful and non-misleading speech, regardless of the speaker and regardless of whether the speech is intended to be 'promotional' or'educational', is constitutionally protected when accompanied by adequate disclosures. In the absence of a legislative and/or regulatory overhaul to FDA's drug promotion regime, the next lawsuit challenging FDA could very well lead a court to hold FDA's entire regime unconstitutional. We believe that if a court were to extend the rationale of *Caronia* and *Amarin* to its logical conclusion in a facial challenge to FDA's existing regime, then FDA would not be able—consistent with the First Amendment—to prosecute off-label speech or even speech that is not supported by 'substantial evidence'[13] 'unless' FDA could establish that such speech is actually false or misleading.

---

4 2015 WL 4720039, at *1 (S.D.N.Y. Aug. 7, 2015).
5 *Id.*
6 *Id.*
7 *Id.* at 24.
8 Alan Bennett et al., *Back to First Principles: A New Model for Drug Promotion*, 2 J. L. & Biosci. 168, 171 (2015).
9 *Id.* at 25.
10 See Compl., Pacira Pharms., Inc. v. FDA, No. 15-cv-07055 (S.D.N.Y. Sept. 8, 2015).
11 *Id.*
12 See Stip. & Order, Pacira Pharms., Inc. v. FDA, No. 15-cv-07055 (S.D.N.Y. Dec. 15, 2015).
13 See Bennett et al., *supra* note 8, at 183, 185.

This type of judicial overhaul would likely result in a system where all drug manufacturer speech is permissible, so long as it is truthful and non-misleading. Although a basic truthful and non-misleading standard would certainly protect drug manufacturers' First Amendment rights, it would likely not achieve all of the objectives of our New Model[14] and may not protect the interests of healthcare professionals and payors, public health advocates, academics, or, for that matter, even industry stakeholders. Among other potential weaknesses, a truthful and non-misleading standard for all drug manufacturer speech would not necessarily promote the development of new uses for drugs. Moreover, such a standard would not necessarily serve the public health, given the potentially unlimited amount of information that could be disseminated to healthcare professionals and payors and the unlimited types of evidence and levels of substantiation upon which manufacturers could rely to support such communications.

Our New Model proposes a more nuanced approach to drug regulation than a regime with only a truthful and non-misleading standard. The level of regulation provided FDA for each category of speech under the New Model is associated with the strength of the government's interest in regulating the specific communications included within each category and the immediacy of the commercial transaction being proposed. We believe the New Model would be preferable to a basic truthful and non-misleading standard because the New Model should help protect the public health while maintaining appropriate incentives for manufacturers to develop and study new uses. At the same time, the New Model would better align the FDA's policies with the First Amendment because the New Model is based on the premise that FDA may, consistent with the First Amendment, set reasonable limits on well-defined categories of commercial speech, provided that meaningful and clear alternative avenues of communication remain open.

Under the New Model, we proposed that Scientific Exchange, which we defined as communications that are intended to advance the scientific enterprise, would not be subject to regulation by FDA. Both Krause and Zettler expressed concerns about exempting Scientific Exchange from FDA regulation given potential difficulties in distinguishing between scientific-focused and commercial-focused communications. Referencing alleged promotional abuses in the pharmaceutical industry, Krause questioned the fundamental premise that scientific information provided by drug manufacturers could be 'trustworthy'.[15] Zettler also worried that exempting Scientific Exchange from FDA regulation would not protect the public health.[16]

In response to the concerns of Krause and Zettler, we wish to emphasize two points. First, one cannot paint the entire pharmaceutical industry with a broad brush and assume that scientific communications by drug manufacturers are inherently misleading or manipulative. Whether one agrees or disagrees with the practices of pharmaceutical manufacturers is largely irrelevant to the question of whether the current regulatory framework is constitutional. Assuming that all drug manufacturer communications are untrustworthy and misleading would fly in the face of the First Amendment as a constitutional matter, and it would also fail to protect the public health as a policy matter,

---

[14] See *id.* at 190.

[15] See Krause, *supra* note 1, at 6, 7.

[16] See Zettler, *supra* note 2, at 4, 5.

given that manufacturers are generally in the best position to communicate up-to-date information about their own drugs.[17]

Second, the formulation of Scientific Exchange set forth in the New Model is actually rather narrow and includes important protections and disclosure requirements. We acknowledge that there may be difficulties in distinguishing Scientific Exchange from other promotional communications in certain cases, but we believe this distinction is appropriate. Under the New Model, a communication would only qualify as Scientific Exchange if (i) it advances the systematic pursuit of knowledge and occurs among only sophisticated, highly educated, and experienced entities; (ii) the information is factual, scientific, and data-driven; (iii) the information is placed in the appropriate context, *and* (iv) it does not include conclusions or promotional claims about the safety or effectiveness of a drug for a particular use. We believe that this narrow formulation would mean that many drug manufacturer communications would not qualify as Scientific Exchange and would therefore still be subject to some form of FDA regulation.

We continue to believe that healthcare professionals, payors, and industry stakeholders would benefit from the implementation of a new regulatory framework for drug promotion, such as the New Model. Given recent court decisions in *Caronia* and *Amarin* that have confirmed drug manufacturers' First Amendment rights, there is an urgent need for action by policymakers to update FDA's drug promotional regime before a court completely upends the current regime.

[17] See Bennett et al, *supra* note 8, at 193.