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Regulating drug promotion to promote the public health: a response to Bennett et al.

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In *Back to First Principles: A New Model for the Regulation of Drug Promotion*, Alan Bennett and co-authors rightly argue that it is time for the U.S. Food and Drug Administration (FDA) to reconsider its scheme for regulating prescription drug promotion.¹ Bennett and his co-authors assert that the FDA's framework for overseeing prescription drug promotion is outdated because it was developed over 50 years ago when communication techniques and technologies, and First Amendment jurisprudence regarding protections for commercial speech, were appreciably different.² Indeed, as Bennett and colleagues note, the FDA itself appears to agree that change, or at least clarification, may be warranted. For example, in recent years, the FDA has held or announced public meetings to solicit stakeholder input, announced a number of studies of drug promotion, and has issued several draft guidance documents intended to clarify certain aspects of its regulation of prescription drug promotion.³

Bennett and colleagues propose a 'New Model' to modernize the FDA's regulatory scheme. The New Model would create three categories of drug manufacturer

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¹ Alan Bennett et al., *Back to First Principles: A New Model for Drug Promotion*, 2 J. LAW BIOSCL. 168, 169–70 (2015).

² *Id.*

³ See eg *Notice of Public Hearing: Promotion of FDA-Regulated Medical Products Using the Internet and Social Media Tools*, 74 Fed. Reg. 48,083 (Sept. 21, 2009); Bennett et al., *supra* note 1, at 186, 189; Toni Clark, *Under Pressure, FDA to Hold Public Meeting on Off-Label Use*, REUTERS (May 6, 2015), <http://www.reuters.com/article/2015/05/07/us-fda-pharmaceuticals-constitution-idUSKBNONS00F20150507>; Alexander Gaffney, *Is FDA Laying the Groundwork for a Broad Shift in the Way It Regulates DTC Drug Advertising?*, REG. AFF. PROFF. SOC'Y (Dec. 2, 2013), <http://www.raps.org/focus-online/news/news-article-view/article/4372/is-fda-laying-the-groundwork-for-a-broad-shift-in-the-way-it-regulates-dtc-drug.aspx>.

communications—(1) Scientific Exchange and Other Exempt Communications, (2) Non-Core Communications, and (3) Core Communications—with the first category being exempt from FDA oversight, the second subject to some FDA oversight, and the third category subject to the most stringent FDA oversight.⁴ The New Model is intended to address concerns that the FDA’s current regulatory scheme violates the First Amendment rights of drug manufacturers, to establish clear rules for drug manufacturers, and to serve the FDA’s public health mission—by increasing the amount of accurate information about drugs available to the public, maintaining the integrity of the FDA’s approval process, and maintaining incentives for drug manufacturers to study new uses of their products.⁵

I agree with Bennett and colleagues that these are key goals for any reform to FDA oversight of prescription drug promotion, and their New Model is a thoughtful proposal to achieve these goals. But, leaving aside the obviously important question of whether the New Model would, in fact, address concerns that the FDA’s regulatory scheme violates drug manufacturers’ First Amendment rights,⁶ this commentary explores whether the New Model would serve its other aims of providing clear rules for drug manufacturers and serving the public health. To that end, I raise some questions about whether the New Model would accomplish those two aims, primarily focusing on the proposal to categorically exempt scientific and certain other communications from FDA oversight.

As a preliminary matter, whatever one thinks of the substance of the FDA’s current regulatory scheme, it arguably is not the case that the FDA’s existing requirements are generally unclear to drug manufacturers. As Bennett and co-authors note, the FDA’s requirements have been in place for over 50 years, giving drug manufacturers extensive experience with how the FDA interprets and implements those requirements. Additionally, it does not appear that the FDA identifies an overwhelming number of violations in this area, which might be expected if there were widespread misunderstanding of the FDA’s requirements. In 2014, the FDA’s Office of Prescription Drug Promotion (OPDP) sent only 10 warning or untitled letters.⁷ Even considering the higher number of OPDP warning and untitled letters in previous years (eg 24 in 2013, and 28 in 2012), the number of FDA actions is not particularly high when compared to the number of drugs that are marketed, and the estimated 27 billion dollars that the pharmaceutical

⁴ See Bennett et al., *supra* note 1, at 202, 212.

⁵ See *id.* at 190.

⁶ It is worth noting that in the short time since Bennett et al.’s article was published, there have been some legal developments with respect to the First Amendment and FDA regulation of drug promotion. See eg *Amarin Pharma Inc. v. FDA*, No. 15-CV-03588 (S.D.N.Y. Aug. 7, 2015).

⁷ U.S. FOOD & DRUG ADMIN., Warning Letters and Notice of Violation Letters to Pharmaceutical Companies, <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/default.htm> [hereinafter ‘FDA Warning Letters’]. A warning letter is an ‘informal and advisory’ communication that is not a final agency action, which the FDA sends to firms to give them an opportunity to voluntarily correct violations of the law. The FDA sends a warning letter for violations ‘of regulatory significance’. An untitled letter is similar to a warning letter, but is sent when violations ‘do not meet the threshold of regulatory significance’. Accordingly warning and untitled letters are advisory rather than enforcement actions—but they do provide a means to gauge how many violations of the law the FDA has identified. U.S. FOOD & DRUG ADMIN., REGULATORY PROCEDURES MANUAL §§ 4-1, 4-2 (2015), available at <http://www.fda.gov/ICECI/ComplianceManuals/RegulatoryProceduresManual/default.htm>.

industry spends yearly on drug promotion.⁸ Of course, the relatively low number of identified violations might demonstrate that the FDA lacks resources to enforce its requirements, that the FDA has grown more cautious in enforcing its drug promotion requirements in light of recent First Amendment decisions, or that industry speech is broadly chilled by confusion about FDA requirements. But another implication might be that there is not much confusion within industry about what the FDA requires.

That said, it likely is less clear to industry how (or whether) the FDA intends to revise its requirements to explicitly address developments in First Amendment jurisprudence. It also may not be obvious how the FDA intends to apply its requirements to relatively new forms of communication, like social media, for which there is limited regulatory history to instruct stakeholders. Assuming that the FDA's current scheme is unclear—either generally, or in specific, but important, contexts such as social media—the question, then, is would the New Model provide more clarity than what currently exists.

Bennett and colleagues note that 'scientific exchange' is one category of communications that already exists in the FDA's regulations, but that the FDA has not provided a specific, binding definition of 'scientific exchange'.⁹ Drug manufacturers, thus, are left to 'read the tea leaves'.¹⁰ But as Bennett and co-authors acknowledge, undefined terms exist in many agencies' regulatory schemes, and, even considering only the FDA, a lack of specificity is not unique to the drug promotion aspect of the FDA's regulatory scheme. Given this, and other commentators' concerns about the proliferation of vague standards and non-binding guidance at the FDA and other agencies,¹¹ it is not clear whether creating more categories of communication that would require the FDA to draw more lines and establish more definitions, would achieve the authors' goal of creating certain rules for drug manufacturers—or would simply create more tea leaves for drug manufacturers to read.

Moreover, although Bennett and colleagues have provided a reasonable definition of what should constitute scientific exchange or otherwise exempt communications, the FDA may not have provided a general definition of 'scientific exchange' because what constitutes scientific exchange is likely to be highly dependent on the facts of the particular situation. *United States v. Harkonen* provides a useful example.¹² In that case, the government prosecuted Dr. Harkonen, the CEO of a drug company, alleging that

⁸ FDA Warning Letters, *supra* note 7; The PEW Charitable Trusts, Fact Sheet, Persuading the Prescribers: Pharmaceutical Industry Marketing and its Influence on Physicians and Patients, <http://www.pewtrusts.org/en/research-and-analysis/fact-sheets/2013/11/11/persuading-the-prescribers-pharmaceutical-industry-marketing-and-its-influence-on-physicians-and-patients>. It is not clear exactly how many brand-name prescription drugs are currently marketed. But one study estimates that FDA has approved approximately 1400 new molecular entities throughout its history, and, if one includes both brand-name and generic prescription drugs, the FDA estimates there are currently as many as 22,000 approved drugs. Development and Distribution of Patient Medication Information for Prescription Drugs; Public Hearing, 75 Fed. Reg. 52,765, 52,766 (Aug. 27, 2010); Michael Kinch et al., *An Overview of FDA-Approved New Molecular Entities 1827-2013*, 19 DRUG DISCOV. TODAY 1033, 1034 (2014).

⁹ See Bennett et al., *supra* note 1, at 186; see also 21 C.F.R. § 312.7(a) (2015) ("This provision is not intended to restrict the full exchange of scientific information concerning the drug...").

¹⁰ *Id.*

¹¹ See eg Lars Noah, *Governance by the Backdoor: Administrative Law (lessness?) at the FDA*, 93 NEB. L. REV. 89 (2014); Stephen M. Johnson, *Good Guidance, Good Grief!*, 72 MO. L. REV. 695, 696 (2007).

¹² *United States v. Harkonen*, 510 F. App'x 633, 635 (9th Cir.) *cert. denied*, 134 S. Ct. 824 (2013); see also Stephanie M. Greene, *After Caronia: First Amendment Concerns in Off-Label Promotion*, 51 SAN DIEGO L. REV. 645, 684–89 (2014) (describing *Harkonen*).

he and others at the company fraudulently misrepresented in a press release the results of a phase III trial of a new indication for an approved drug. On its face, the press release looks much like scientific exchange. Indeed, the press release did not involve fabricated or falsified data, nor was the description of the study results objectively false. However, the study discussed in the press release failed to yield any statistically significant results for its pre-defined endpoints, and the positive results reported in the press release were based on unblinded post-hoc analyses. Ultimately, a jury convicted Dr. Harkonen of wire fraud, and the Ninth Circuit upheld that conviction in an unpublished opinion.

Regardless of whether one agrees that Dr. Harkonen should have been convicted, his case demonstrates how fact-intensive an inquiry into whether a communication constitutes legitimate scientific exchange can be¹³—and thus how difficult it may be to write a general definition that can provide significantly greater certainty for industry. Bennett and co-authors might respond that the press release at issue in *Harkonen* would not meet their definition of scientific exchange because the limitations of the post-hoc analyses were not made clear and therefore the information in the press release was not ‘placed in the appropriate context’.¹⁴ But the fact that some scientists and other academic commentators supported Dr. Harkonen and expressed concern that his conviction punishes legitimate scientific communications,¹⁵ suggests that even within the scientific community it may be difficult to generally define scientific exchange.

The difficulty of defining what is or is not legitimate scientific exchange, in turn, raises the question of whether the public health would be served by categorically excluding certain drug manufacturer communications from FDA oversight. Experience and research suggest that drug manufacturers can use scientific or educational communications to market their products. *Harkonen* provides one example. Evidence presented at Dr. Harkonen’s trial suggested that the data were presented in an inappropriately positive light in the press release in order to increase off-label sales of the drug. Additionally, concerns have been raised about industry-supported Continuing Medical Education (CME) programs, even when industry sponsors do not expressly control the content of the CME programs.¹⁶ For instance, some (although not all) research has suggested that industry-supported CME programs place more focus on drug treatments and give more favorable treatment to sponsors’ products than do those that are not funded by industry, and that industry receives an approximately 3-fold return on its investment in educational programs.¹⁷ Moreover, as other commentators have

¹³ Cf. *United States v. Harkonen*, No. C 08-00164 MHP, 2010 WL 2985257, at *3 (N.D. Cal. July 27, 2010) (noting that to evaluate the parties’ arguments ‘it is necessary to provide significant detail about the . . . Phase III trial’).

¹⁴ Bennett et al., *supra* note 1, at 203.

¹⁵ See eg Brief for Scientists and Academics as Amici Curiae Supporting Petitioner, *Harkonen v. U.S.*, 2013 WL 5915131 (U.S.) (No. 13-180).

¹⁶ See eg STAFF OF S. FIN. COMM., 110TH CONG., USE OF EDUCATIONAL GRANTS BY PHARMACEUTICAL MANUFACTURERS (Comm. Print 2007); INST. OF MED., CONFLICT OF INTEREST IN MEDICAL RESEARCH, EDUCATION, AND PRACTICE 122-66 (2009).

¹⁷ See eg *Commercial Sponsorship of Continuing Medical Education: Hearing Before the S. Special Comm. on Aging*, 111th Cong. 111-305 (2009) (statement of Lewis Morris, Chief Counsel, Office of Inspector General, Department of Health and Human Services) (describing various studies); but see Michael A. Steinman et al., *Commercial Influence and Learner-Perceived Bias in Continuing Medical Education*, 85 ACAD. MED. 74 (2010) (finding that rates of perceived bias did not differ between industry-supported and noncommercial CME programs).

explained, marketing research suggests that there are emotional and non-conscious ways to convey information in a persuasive manner.¹⁸ Color choice provides one illustration of non-informational means of persuading—for example, green packaging may lead consumers to conclude that products are environmentally friendly.¹⁹ This research indicates that factually and contextually accurate scientific or educational information may nevertheless be finessed.

This not to say that there is no public health value in drug manufacturers' scientific and educational communications. As Bennett and co-authors explain, drug manufacturers often have the most extensive and up-to-date information about their products, and, as a general matter, I agree with the authors that allowing the public to access that information might have some positive public health effects. But I am more skeptical of the relative public health value of drug manufacturer communications than the authors appear to be. Given the difficulty of defining a general category of scientific (and other exempt) communications, and the reality that even communications that meet Bennett and colleagues' very reasonable definition of scientific exchange might be manipulative, 'scientific exchange' may not be the most useful line to draw from the public health perspective.

¹⁸ See eg Micah L. Berman, *Manipulative Marketing and the First Amendment*, 103 GEO. L.J. 497, 532 (2015).

¹⁹ See *id.*