Up to Their Old Devices? Why Differences in Drug and Device Promotion Standards Matter From An Enforcement Perspective

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While pharmaceutical manufacturers have been the most common target of government investigations for violations of advertising and promotion rules, prosecutors and other government enforcement officials have predicted an increased enforcement focus on medical device manufacturers. In 2010, the Food and Drug Administration's (FDA) Center for Device and Radiological Health (CDRH) announced that its Office of Compliance had increased the size of its device advertising and promotion policy group from one person to three, and that the Office expected a concomitant increase in advertising and promotion enforcement efforts as well as policy development.[1] In late 2012, the Department of Health and Human Services Office of Inspector General's (OIG) top enforcement officials predicted an uptick in marketing-related False Claims Act (FCA) cases against medical device manufacturers.[2]

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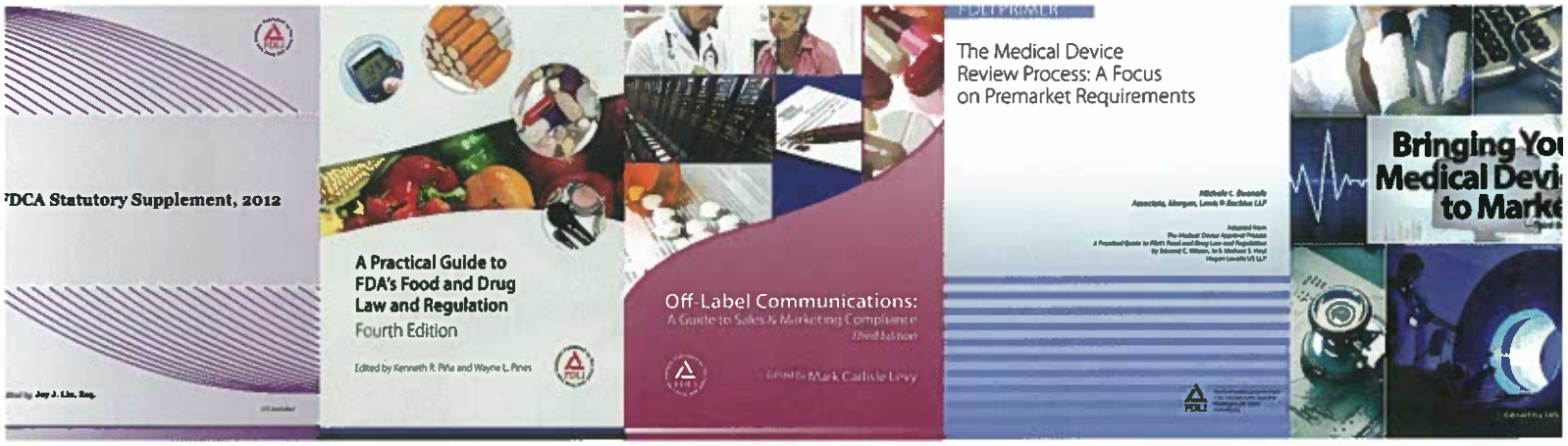

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These pronouncements raise concerns that FDA, the OIG and the Department of Justice (DOJ) will pursue marketing and promotion-related actions against medical device manufacturers based on theories similar to those employed against pharmaceutical manufacturers. In reality, however, significant differences exist in the relevant law and regulations applicable to the advertising and promotion of medical devices as compared to pharmaceuticals.[3] These differences have led to a striking lack of guidance regarding the parameters of permissible medical device promotion. In exercising their enforcement discretion, prosecutors and regulatory officials should be mindful of these differences, as well as the inherent unfairness of prosecuting violations of ambiguous legal and regulatory requirements.

The Relevant Statutory and Regulatory Framework Offer Little Guidance Regarding Medical Device Promotion

The Food, Drug, and Cosmetic Act (FDCA) generally provides that a "drug or device shall be deemed to be misbranded . . . [i]f its labeling is false or misleading in any particular."[4] The statute defines labeling to include any "written, printed, or graphic matter" (1) upon a drug itself, its immediate or other "containers or wrappers," or (2) "accompanying such article."[5] In *Kordel v. United States*, the Supreme Court broadly interpreted the term "labeling" to include "literature . . . designed for use in the distribution and sale of [a] drug" but not part of the drug's packaging.[6] Accordingly, pursuant to FDA regulations, "labeling" encompasses a broad variety of printed or written materials supplied by a manufacturer, packer or distributor, or disseminated on behalf of a manufacturer or distributor.[7]

FDA has jurisdiction over all drug and medical device labeling, including "promotional labeling," a term which FDA uses but does not differentiate from "labeling" as defined in the FDCA and related regulations.[8] In determining whether a drug or device is misbranded due to misleading labeling, FDA takes into account not only representations made about the drug or device, "but also the extent to which the labeling . . . fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article . . . under the conditions of use prescribed in the labeling or advertising . . . or under such conditions of use as are customary or usual."[9]

This is where the similarities between regulation of drug and device promotion largely cease. As an initial matter, while FDA has complete jurisdiction over prescription drug labeling and advertising, as well as all medical device labeling, it has limited jurisdiction over medical device advertising. FDA is only authorized to regulate the advertising of "restricted" medical devices.[10] Restricted devices represent a subset of medical devices, which is not coextensive with prescription medical devices. Most Class III premarket approval devices have been restricted as a condition of approval, but only a few Class I and Class II devices (such as hearing aids) are restricted by regulation.[11] The advertising of all non-restricted medical devices – the majority of marketed medical devices – is regulated by the Federal Trade Commission under Sections 12-15 of the Federal Trade Commission Act.[12]

Perhaps because of this split in oversight, FDA has issued far less regulation and guidance regarding medical device promotion than regarding prescription drug promotion. The FDCA includes just two specific provisions regarding restricted device advertising: 21 U.S.C. § 352(q) provides that a restricted device is misbranded if its advertising is false and misleading in any particular, and 21 U.S.C. § 352(r) provides that a restricted device is misbranded if its advertising does not contain a brief statement of the device's intended use and relevant warnings precautions, side effects and contraindications. FDA has not promulgated any regulations relating to medical device promotion or advertising, nor has it issued any final or draft guidance documents specific to medical device promotion or advertising. Two current draft guidances address promotion and advertising of both prescription drugs and restricted medical devices.[13]

In contrast, FDA has promulgated ten additional guidance documents relating to prescription drug advertising. These guidances supplement FDA's detailed regulations regarding prescription drug advertising, which provide that such advertisements may not be false or misleading or omit materials facts, and must present a fair balance between benefit and risk information.[14] FDA's regulations identify twenty types of prescription drug advertising communications that FDA considers "false, lacking in fair balance, or otherwise misleading,"[15] as well as thirteen additional types of advertising communications that may be "false, lacking in fair balance, or otherwise misleading."[16] "By contrast, FDA's device regulations do not contain specific requirements regarding the content of advertisements for restricted devices. Regulation of restricted device advertising thus stems directly from" the FDCA sections discussed above.[17]

The lack of formal guidance and regulations relating to medical device promotion and advertising is compounded by the dearth of publicly available warning and untitled letters relating to medical device promotion and advertising. This may stem from another significant distinction in the regulation of drugs and devices: unlike with prescription drugs, there is no statutory requirement that device advertisements and promotional material be submitted to FDA at the time of initial dissemination.[18] Moreover, the Office of Prescription Drug Promotion (OPDP) within FDA's Center for Drug Evaluation and Research includes more than 60 personnel devoted to "assuring prescription drug information is truthful, balanced and accurately communicated [through] a comprehensive surveillance, enforcement and education program. . . ."[19] Restricted device promotion, in contrast, is reviewed by the CDRH Office of Compliance which, as noted above, recently increased the staff devoted to such review from one to three. As a result, far fewer warning and untitled letters are publicly available regarding medical device promotion and advertising than drug promotion.[20]

Fewer publicly available warning and untitled letters, in turn, results in significantly less guidance for industry to consider. As a practical matter, the warning and untitled letters published on OPDP's website provide the pharmaceutical industry with helpful insight into how FDA believes its statutory and regulatory authority applies in the real world. For example, FDA's prescription drug advertising regulations provide that promotional materials may be deemed misleading if they represent or suggest that a drug is safer than another drug when that has not been demonstrated by substantial evidence or substantial clinical experience.[21] Substantial evidence is defined by statute as:

> evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.[22]

Pursuant to formal guidance, FDA generally requires at least two adequate and well-controlled studies, each convincing on its own, to constitute substantial evidence.[23] FDA may also consider "data from one adequate and well-controlled clinical investigation and confirmatory evidence" to constitute substantial evidence if FDA determines that such data and evidence are sufficient to establish effectiveness.[24] In published warning and untitled letters addressing comparative claims, however, FDA goes beyond this baseline requirement for substantial evidence and asserts that comparative claims must be supported by two adequate, well-controlled head-to-head clinical trials.[25] By articulating this requirement in multiple warning and untitled letters, FDA has introduced a higher standard for prescription drug promotional materials containing comparative claims without issuing guidance or regulation. Absent a similar body of published untitled and warning letters to look to, medical device manufactures can only wonder whether FDA would apply the same standard to restricted medical device promotion.

The muddy landscape created by the lack of clear FDA guidance regarding medical device promotion is further complicated by the FDA/FTC jurisdictional split described above. While the FTC's standards for "false advertising" in many respects track the requirements in FDA's prescription drug advertising regulations, there are significant differences. For instance, the FTC requires certain health-related advertising claims to be substantiated by "competent and reliable scientific evidence," a standard generally recognized as more flexible and "allowing a broader range of claims" than FDA's substantial evidence standard.[26] Similarly, the FTC does not require "fair balance," as that term is strictly defined by FDA, but holds advertisements to a "reasonable" standard of truthfulness.[27] As such, non-restricted device advertisements may be subjected to quite different standards than those FDA would presumably apply to restricted device advertisements.

Absent Clear Guidance, Increased Enforcement May Be Inappropriate

To the extent prosecutors and other government enforcement officials are focusing additional scrutiny on the medical device industry, they should be mindful of the critical lack of guidance available to medical device manufacturers regarding advertising and promotion. It would be inherently unfair to establish new advertising and promotion rules through FDA enforcement action (such as warning and untitled letters) rather than through either notice-and-comment rulemaking or the formal FDA guidance process, which includes an opportunity for comment by interested parties. It would be even more unjust if such standards were established through DOJ criminal and civil enforcement actions. In particular, because the vast majority of such

actions end in negotiated settlements, companies and individuals are left in the difficult position of attempting to read the tea leaves of publicly available settlement documents to determine what is – and is not – permitted, and to adjust their conduct accordingly.

Government enforcement officials also should be mindful of the government's litigation track record in cases involving promotional speech. While FDA has not always agreed, courts have consistently found such speech to be entitled to First Amendment protection insofar as it is truthful and not misleading.[28] As a result, the government bears the burden of demonstrating that laws restricting speech are consistent with the First Amendment.[29] Significantly, in the recent high-profile *U.S. v. Caronia* case, the United States Court of Appeals for the Second Circuit rejected the government's attempt to criminalize truthful, non-misleading speech regarding unapproved uses of prescription drugs.[30] Courts also have rejected FDA's arguments that speech is false or misleading simply because it does not meet FDA's narrow definitions of those terms or has not been approved by FDA.[31] FDA, and DOJ, should bear these precedents in mind when considering whether to pursue enforcement action based on non-statutory interpretations of the statutory "false and misleading" standard applicable to medical device promotion.

Finally, it is important to note that, unlike the majority of laws carrying criminal penalties, the FDCA has been interpreted as a nearly strict-liability statute.[32] To prove a criminal violation of the FDCA, the government is not required to prove "awareness of some wrongdoing" or "conscious fraud."[33] Coupled with the distinct lack of guidance defining what constitutes "false and misleading" medical device promotion, the low legal bar for criminal liability counsels heavily in favor of judicious use of the government's enforcement authority in this area. ⚠

1. *See* http://www.medicaldevicestoday.com/2010/09/device-center-increases-advertisingpromotion-enforcement-staff-.html.
2. *See* http://www.hlregulation.com/2012/11/28/updates-from-fdlis-advertising-promotion-conference-and-the-pharmaceutical-regulatory-compliance-congress.
3. This article focuses on the divergent standards applicable to pharmaceutical and medical device advertising, which is only one of many significant distinctions between the two industries that drive their relative enforcement risks. Other key differences between pharmaceuticals and medical devices include product life cycle and frequency of product modifications, the nature of manufacturers' interactions with health care providers and the need for product training, and applicable reimbursement methodologies.
4. 21 U.S.C. § 352(a).
5. *Id.* § 321(m).
6. 335 U.S. 345, 350 (1948).
7. 21 C.F.R. Part 202.1(l)(2).
8. *See, e.g.,* FDA, Draft Guidance for Industry, "Help-Seeking and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms," (Jan. 2004), *available at*: http://www.fda.gov/downloads/ Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070068.pdf .
9. 21 U.S.C. § 321(n).
10. 21 U.S.C. §§ 352(q) and 352(r). Medical devices may become restricted in one of three ways: (1) FDA may by regulation restrict a device to sale, distribution or use only upon authorization of a practitioner licensed by law to administer or use such device, or upon conditions that FDA prescribes in the regulation, if FDA determines there cannot otherwise be reasonable assurance of the device's safety and effectiveness, 21 U.S.C. § 360j(e); (2) FDA may require, as a condition of approval of a Class III device, that its sale and distribution be restricted, *id.* § 360e(d)(1)(B)(ii); and (3) FDA may establish, as part of a performance standard, requirements that the sale and distribution of a device be restricted, *id.* § 360d)(a)(2)(b)(v).
11. FDA Oversight of Direct-to-consumer Advertising of Medical Devices, Statement of Daniel Schultz, M.D., Director of CDRH before the Senate Special Committee on Aging (Sept. 17, 2008), *available at* http://www.fda.gov/NewsEvents/Testimony/ucm096272.htm ("FDA Testimony").
12. 15 U.S.C. §§ 52-55.
13. FDA, Draft Guidance for Industry, "Help-Seeking and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms," (Jan. 2004), *available at*: http://www.fda.gov/downloads/ Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070068.pdf ; and Draft Guidance for Industry, "Presenting Risk Information in Prescription Drug and Medical Device Promotion," (May 2009), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ UCM155480.pdf. A third draft guidance, relating to consumer-directed broadcast advertisements for restricted medical devices, was withdrawn in September 2012.
14. *See* 21 C.F.R. Part 202.1.
15. *Id.* Part 202.1(e)(6).
16. *Id.* Part 202.1(e)(7).
17. FDA Testimony.
18. *See* 21 C.F.R. Part 314.81(b)(3)(i).
19. *See* OPDP Mission, *available at* http://www.fda.gov/AboutFDA/CentersOffices/ OfficeofMedicalProductsandTobacco/CDER/ucm090142.htm; OPDP Organization Listing, *available at* http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm154886.htm.
20. Although CDRH's website indicates that "[a]s part of [FDA's] Transparency Initiative, CDRH has committed to posting its advertising and promotion Untitled Letters from October 1, 2011," the only untitled letter available on the website is a February 2013 email untitled letter jointly issued by FDA and FTC to manufacturers of decorative contact lenses. The email advises that: (1) the lenses may be adulterated and misbranded in violation of the FDCA if they are offered for sale without FDA marketing authorization; and (2) the sale of contact lenses to consumers without a valid prescription is in violation of the Fairness to Contact Lens Consumers Act, 15 U.S.C. § 7601 *et seq.*, and the

Contact Lens Rule, 16 C.F.R. Part 315, both of which are enforced by the FTC. The email does not specifically address advertising or promotion of the contact lenses. *See* http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/ucm111104.htm.

21. 21 C.F.R. Part 202.1(e)(6)(ii).
22. 21 U.S.C. § 355(d).
23. FDA, Guidance for Industry, "Providing Clinical Evidence Guidance of Effectiveness for Human Drug and Biological Products" (May 1998), at 3, *available at* http://www.fda.gov/downloads/Drugs/ GuidanceComplianceRegulatoryInformation/Guidances/UCM078749.pdf.
24. 21 U.S.C. § 355(d).
25. *See, e.g.*, Untitled Letter to Dow Pharmaceutical Sciences, Inc. (Mar. 3, 2012); Warning Letter to Novartis Pharmaceuticals (Aug. 8, 2007).
26. FTC Comments on First Amendment Issues, FDA Docket No. 02N-0209 (Sept. 13, 2002) ("FTC Comments"), at 3, *available at* http://www.ftc.gov/os/2002/09/fdatextversion.pdf. *See also id.* at 17 (The standard is defined in FTC cases to mean "'tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.' The competent and reliable scientific evidence standard is intended to be rigorous but not inflexible. It provides some leeway to ensure that consumers have access to truthful, well-qualified information about emerging areas of science, while at the same time ensuring that consumers can have confidence in the accuracy of claims.") (citing *Schering Corp.*, 118 F.T.C. 1030 (1994) (consent) (challenging unsubstantiated weight loss claims for Fibre Trim supplement); *Interstate Bakeries Corp.*, C-4042 (2002) (consent) (challenging unsubstantiated brain function and memory claims for Wonderbread); *Pfizer, Inc.*, C-3841(1998) (consent) (challenging unsubstantiated efficacy claims for head lice treatment)). "While the FTC has recently employed more demanding standards for disease and health-related claims regarding food and dietary supplements, it still employs the "competent and reliable scientific evidence" standard for other product-related claims." *See FTC v. Iovate Health Scis. USA, Inc.*, Case. No. 10-CV-587 (W.D.N.Y. July 29, 2010) (Stipulated Final Judgment); *Nestlé HealthCare Nutrition, Inc.*, FTC File No. 092-3087, Agreement Containing Consent Order (July 14, 2010).
27. FTC Comments at 15 ("The Commission will examine whether an ad omits any important qualifying information necessary to prevent an affirmative representation from being misleading. Advertising may also be deceptive by simply remaining silent, if doing so communicates an implied, false representation. Not all omissions are deceptive, however, even if providing the information would benefit consumers. An omission is deceptive only if the absence of the information causes the advertisement to give the audience an inaccurate impression of the product and its benefits.") (citations omitted).
28. In *Sorrell v. IMS Health, Inc.*, the Supreme Court specifically held that "[s]peech in aid of pharmaceutical marketing . . . is a form of expression protected by the Free Speech Clause of the First Amendment." 131 S. Ct. 2653, 2659 (2011). In particular, the Court held that a Vermont statute "that disfavored speech with a particular content (marketing) when expressed by certain disfavored speakers (pharmaceutical manufacturers) . . . unconstitutionally restricted speech. *Id.* at 2662-65, 2672; *see also U.S. v. Caronia*, 703 F.3d 149, 163 (2012) (citing *Sorrell*).
29. *Sorrell*, 131 S. Ct. at 2667 (citing *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 373 (2002)).
30. *See generally Caronia*, 703 F.3d 149.
31. *See Pearson v. Shalala*, 164 F.3d 650, 655 (1999) (rejecting FDA argument that health claims lacking "significant scientific agreement" are "inherently misleading"); *Washington Legal Foundation v. Friedman*, 13 F.Supp.2d 51, 67 (D.D.C. 1998) ("In asserting that any and all scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs are presumptively untruthful or misleading until the FDA has had the opportunity to evaluate them, FDA exaggerates its overall place in the universe.")
32. *United States v. Dotterweich*, 320 U.S. 277, 280-81 (1943) (The FDCA "dispenses with the conventional requirement for criminal conduct -- awareness of some wrongdoing. In the interest of the larger good it puts the burden of acting at hazard upon a person otherwise innocent but standing in responsible relation to a public danger."); *United States v. Park*, 421 U.S. 658, 672-73 (1975) ("The Act does not, as we observed in *Dotterweich*, make criminal liability turn on 'awareness of some wrongdoing' or 'conscious fraud.' The duty imposed by Congress on responsible corporate agents is, we emphasize, one that requires the highest standard of foresight and vigilance, but the Act, in its criminal aspect, does not require that which is objectively impossible.") (citing *Dotterweich*, 210 U.S. at 280-281).
33. *Id.*