

FDA Proposes a Restrictive Framework for Regulating Requests for Medical Product Information

On December 30, 2011, the US Food and Drug Administration (FDA) released for public comment a draft guidance titled, “Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices” (Draft Guidance).¹ The Draft Guidance provides FDA’s nonbinding positions on how human and animal drug and medical device manufacturers should respond to unsolicited requests for information about unapproved or uncleared uses (off-label uses) of FDA-regulated products. The Draft Guidance proposes to distinguish between standards governing “public” and “non-public” responses to off-label questions and specifies the circumstances in which a manufacturer may respond. FDA states that it will refrain from using a manufacturer’s provision of off-label information in response to an unsolicited request, as evidence of an unlawful intended use, if that information is provided in conformance with the Draft Guidance recommendations, including associated documentation requirements. This Draft Guidance, and the highly restrictive framework it proposes for responding to off-label inquiries, raises a number of important legal issues that have the potential to impact how manufacturers engage in such communications, both in live settings and online. The Draft Guidance also represents another example of FDA’s expansive interpretation of its authorities, despite developing First Amendment case law suggesting that the Agency’s actual ability to restrict speech is significantly more limited.

Non-Public Unsolicited Requests

FDA defines “non-public” unsolicited requests as those requests that are directed to a manufacturer “privately using a one-on-one communication approach.”² The Draft Guidance cites one-on-one phone calls, emails, and communications via manufacturer-controlled websites as media through which non-public requests could occur.³ Additionally,

1 FDA, Draft Guidance for Industry—Responding to Unsolicited Requests for Off-Label Information about Prescription Drugs and Medical Devices (Dec. 2011) [hereinafter “Draft Guidance”], available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM285145.pdf>. FDA, Notice of Availability of Draft Guidance, 76 Fed. Reg. 82303 (Dec. 30, 2011), available at <http://www.gpo.gov/fdsys/pkg/FR-2011-12-30/pdf/2011-33550.pdf>.

2 *Id.* at 4.

3 *Id.* at 7.

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the Draft Guidance provides examples of different communications that would be considered “non-public.” For example, an individual who spontaneously calls or e-mails a firm’s medical information staff to seek information about an off-label use would be making a “non-public” unsolicited request.⁴

FDA proposes that responses to non-public requests may include off-label information and will not be used as evidence of an unlawful use or otherwise be subject to requirements for promotional labeling or advertising if the information provided in a given response is:

- (1) Only provided to the individual making the request as a private, one-on-one communication;
- (2) Tailored to answer only the specific question(s) asked;
- (3) Truthful, nonmisleading, accurate, and balanced (such as by providing “non-biased information or data relating to the particular off-label use that is the subject of the request, including applicable data that are not supportive or that cast doubt on the safety or efficacy of that use”);
- (4) Scientific in nature (i.e., not promotional in “tone or presentation”);
- (5) Generated by medical or scientific personnel, independent from sales or marketing departments;
- (6) Accompanied by copies of the FDA-approved labeling, all important safety information, prominent statements disclosing the approved indication and noting that the information contained is not FDA-approved, and a complete list of references for all the information disseminated in the response); and
- (7) Recorded along with the nature of the request and contact information of requestor.⁵

FDA further states that:

[T]he response should include complete copies of scientific reprints, technical literature, or other scientific

and medical information responsive to the request, not just summary documents or abstracts prepared by the firm. The response can include unpublished data on file if they are responsive to the specific request (either supporting or casting doubt on the safety or efficacy of the off-label use). However, to the greatest extent possible, a firm should rely on published peer-reviewed journal articles, medical texts, or data derived from independent sources. To the extent the response consists of published reprints from journals, those reprints should be from journals that have a publicly stated policy, to which the organization adheres, of full disclosure of any conflict of interest or biases for all authors, contributors, or editors associated with the journal or organization.⁶

The Agency’s attempt to dictate the precise nature of a response appears to be overreaching. For example, a strong argument can be made that any balanced and credible response to an unsolicited request satisfies any requirements associated with a *bona fide* scientific, nonpromotional exchange—including a standardized summary of the literature on the topic prepared by a medical affairs function—regardless of whether full reprints are provided.

Public Unsolicited Requests

“Public” unsolicited requests are defined by FDA as requests “made in a public forum, whether directed to a [drug or device manufacturer] specifically or to a forum at large.”⁷ FDA provides two key examples.⁸ First, if an individual asks a manufacturer’s representative a question about an off-label use about a manufacturer’s product during a live presentation (such as a promotional speaker program), the request and the response would be considered “public” if it could be overheard by other attendees. Similarly, if an individual posts a question to a manufacturer-controlled website about a specific product’s off-label use, and the

⁴ *Id.* at 4.

⁵ *Id.* at 7-9. Additional examples of solicited requests are provided in the Draft Guidance at 5-6.

⁶ *Id.* at 8.

⁷ *Id.* at 4.

⁸ *Id.*

question is visible to a broad audience (e.g., a blog entry), then FDA would consider the post to be a “public” request. If a manufacturer chooses to respond in a way that is visible to the same audience (e.g., a public thread in the same blog), then FDA would consider the response to be “public” as well.

FDA has expressed concern about the quality of information available to the public via the Internet and other electronic mass-media.⁹ Consequently, FDA proposes to refrain from initiating enforcement against manufacturers solely on the basis of providing responses to public requests if the information provided in a given response:

- (1) Concerns only responding manufacturer’s own named product (and is not solely about a competitor’s product);
- (2) Conveys that the question pertains to an unapproved use, notes that the requestor can contact the manufacturer’s medical/scientific department for more information, and provides contact information specific to that department;
- (3) Clearly discloses the source of the response and the manufacturer’s involvement; and
- (4) Is not “promotional in nature or tone” and includes a mechanism for providing the FDA-approved product labeling.¹⁰

It should be noted that this framework only applies to public and non-public *unsolicited* requests. As the Draft Guidance notes, “solicited requests may be considered evidence of a firm’s intent that a drug or medical device be used for a use other than that specifically approved or cleared by FDA.”¹¹ The Draft Guidance provides examples of interactions FDA considers to be *solicited* requests for off-label information. For example, if a representative of a firm (such as a medical science liaison or paid speaker) presents data on

an off-label use at a company-sponsored promotional event, any subsequent questions from attendees would be considered to be solicited. The resulting responses from the representative could be used as evidence of the manufacturer’s off-label intent. Similarly, if a manufacturer asked or otherwise encouraged users to post videos about their own uses of its product on third-party video-sharing sites (e.g., YouTube), which could result in video postings about an off-label use of its product, and such postings occurred, then subsequent postings or questions about those postings could be considered as evidence of the manufacturer’s intended use.

Implications for Manufacturers

Congress and FDA have long recognized the public health benefit of allowing manufacturers to engage in scientific exchange with members of the healthcare community and public, as manufacturers often possess the most up-to-date information about safety and efficacy of their products.¹² Moreover, the Agency does not regulate the practice of medicine.¹³ Despite the Agency’s acknowledgement of

⁹ Because “product information posted on websites [...] is likely to be available to a broad audience and for an indefinite period of time,” there is concern that drug and device manufacturers “may post detailed public online responses to questions about off-label uses for their products in such a way that they are communicating unapproved [...] use information about FDA-regulated medical products to individuals who have not requested such information.” *Id.* at 10.

¹⁰ *Id.* at 11-12.

¹¹ *Id.* at 5.

¹² See, e.g., FDA, Notice of Decision in *Washington Legal Found. v. Henney*, 65 Fed. Reg. 14, 286 (Mar. 16 2000) (recognizing that because manufacturers often have more information about a drug’s characteristics and potential utility than health care providers (HCPs) do (including for off-label uses), it is important that FDA permit *bona fide* scientific exchange between a manufacturer and HCPs); Thomas Bliley, Commerce Comm., Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997, H.R. Rep 105-310 (1st Sess. 1997) (report to accompany Food and Drug Administration Modernization Act of 1997, H.R. 1411, 105th Cong. (1997)) (“...[n]othing in section 745 [of the House Bill] shall be construed as prohibiting a manufacturer from disseminating information in response to an unsolicited request from a health care practitioner. The Committee wants to emphasize that current FDA policies that encourage scientific exchange are not being modified ...”).

¹³ See, e.g., *Planned Parenthood of Cincinnati Region v. Strickland*, 531 F.3d 406, 408 (6th Cir. 2008) (“Absent state regulation, once a drug has been approved by the FDA, doctors may prescribe it for indications and in dosages other than those expressly approved by the FDA. This is a widely employed practice known as ‘off-label’ use. Off-label use does not violate federal law or FDA regulations because the FDA regulates the marketing and distribution of drugs in the United States, not the practice of medicine, which is the exclusive realm of individual states”); *Chaney v. Heckler*, 718 F.2d 1174, 1180 n.13 (D.C. Cir. 1983), *rev’d on other grounds*, 470 U.S. 821 (1985) (“[The federal Food, Drug, and Cosmetic Act] legislative history expresses a specific intent to prohibit FDA from regulating physicians’ practice of medicine.”)

scientific exchange and the importance of providing further guidance to manufacturers on off-label questions in an electronic age, the Draft Guidance leaves several important questions unanswered.

Notably, courts have held that the First Amendment limits FDA's ability to regulate scientific speech.¹⁴ Moreover, in its last term, the Supreme Court in *IMS Health Inc. v. Sorrell*, held that a law banning commercial speech based on the content of the speaker's message or the identity of the speaker is subject to "heightened judicial scrutiny."¹⁵ The Court proceeded to invalidate a Vermont law that prohibited pharmaceutical companies from marketing their products while using "prescriber-identifiable data," but that would have permitted other actors in the marketplace (such as insurers or academics) to use "prescriber-identifiable data" for marketing purposes. The *Sorrell* Court rejected paternalism as a basis for restricting truthful and nonmisleading speech, particularly in light of the fact that physicians are highly trained professionals who take an oath to protect the health of their patients. In light of *Sorrell*, there are very real questions about whether FDA can impose the speaker and content restrictions upon information provided in response to unsolicited requests by healthcare professionals. Under logic similar to that applied in *Sorrell*, attempts by FDA to provide "guidance" on such restrictions have been struck down by the courts as impermissible infringements on commercial speech.¹⁶ Responses to unsolicited requests

by healthcare professionals have historically been a paradigmatic example of "bona fide" scientific exchange, and outside of FDA's regulatory jurisdiction, either as evidence of intended use or as labeling/advertising.

The proposed Draft Guidance however, appears to take a step backwards by potentially imposing "promotional labeling-like" requirements, including provision of "fair balance" and financial or editorial disclosures on information historically considered scientific in nature. Notably, these balancing requirements mirror those recommended by FDA in its guidance governing affirmative dissemination of off-label reprints (including by a manufacturer's sales force).¹⁷ It is far from clear that it would be constitutional for FDA to bring enforcement against responses to unsolicited requests that fell short of the standards reflected in this guidance.

While the Draft Guidance suggests that unsolicited requests may properly originate from "health care professionals, health care organization, members of the academic community . . . formulary committees . . . [and] consumers such as patients and caregivers" it is unclear whether responses would need to be tailored to the training and experience level of the particular requestor. Currently, medical information groups at major medical product companies are generally resourced to respond to questions from healthcare professionals, and the information provided is generally technical in nature. Would it be consistent with FDA's policies governing consumer-directed risk communication to provide clinical information to a lay person? Would the provision of such information fall outside the proposed protections offered by compliance with the Draft Guidance?

The Draft Guidance also does not appear to consider whether unsolicited requests for presentations by a manufacturer's medical or managed-care representatives to a formulary committee (or other medical product purchasing body) would be considered "public" or "non-public." Would requests

¹⁴ *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 62 (D.D.C. 1998) amended, 36 F. Supp. 2d 16 (D.D.C. 1999) appeal dismissed, judgment vacated in part sub nom. *Washington Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000) and amended, 36 F. Supp. 2d 418 (D.D.C. 1999) and appeal dismissed, judgment vacated in part sub nom. *Washington Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000). *Bd. Of Trustees of Leland Stanford Jr. Univ. v. Sullivan*, 773 F. Supp. 472, 474 (D.D.C. 1991).

¹⁵ Arnold & Porter LLP was lead counsel for plaintiff Pharmaceutical Research and Manufacturers of America (PhRMA) in *IMS Health Inc. v. Sorrell*, 131 S. Ct. 2653, 2659 (2011). See also Arnold & Porter LLP, "Advisory: Supreme Court Holds that Pharmaceutical Company Promotion Is Entitled to Full First Amendment Protection," (June 2011) available at http://www.arnoldporter.com/public_document.cfm?id=17710&key=4A2.

¹⁶ See, e.g., *Washington Legal Found. v. Henney*, 56 F. Supp.2d 81 (D.D.C. 2000) (finding unconstitutional FDA guidance documents that limited the ability of manufacturers to distribute scientific information and imposed restrictions on protected commercial speech), vacated in part, 202 F.3d 331(D.C. Cir. 2000).

¹⁷ See FDA, Guidance for Industry—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) available at <http://www.fda.gov/oc/op/goodreprint.html>.

for presentations on off-label uses of a manufacturer's product need to be refused in order to comply with the Draft Guidance? This would not seem to be in the interest of science-based managed-care decision making, particularly given the sophisticated nature of such audiences.

Finally, while FDA has provided some helpful examples of how the Internet and electronic media may play a role in public/non-public framework, the Draft Guidance does not address the growing trend by manufacturers to provide "real-time" consultations between doctors and their medical/scientific staff. For example, would it be permissible for a sales representative to respond to a doctor's unsolicited off-label question by making available her iPad® or laptop to immediately patch the doctor through to medical affairs via Skype™?

Given the scrutiny that manufacturer promotional and scientific activities may face and the important First Amendment implications of the guidance, it will be important for manufacturers and other stakeholders to respond to FDA's proposals in a thoughtful manner. Stakeholders must submit comments to FDA on the Draft Guidance by March 29, 2012.

We hope you have found this Advisory useful. Please feel free to contact your Arnold & Porter attorney, or any of the contacts below, if you have further questions:

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