Docket No. FDA-2015-N-2002

COMMENTS

of

WASHINGTON LEGAL FOUNDATION

to the

FOOD AND DRUG ADMINISTRATION
U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Concerning

Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses"

IN RESPONSE TO THE PUBLIC NOTICE PUBLISHED
AT 80 FED. REG. 57756 (Sept. 25, 2015)

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November 24, 2015

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Submitted Electronically (www.regulations.gov)
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Re: Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses"
Docket No. FDA-2015-N-2002, 80 Fed. Reg. 57756 (Sept. 25, 2015)

Dear Sir/Madam:

Washington Legal Foundation (WLF) is pleased to have the opportunity to respond to the Food and Drug Administration's (FDA) proposed regulations regarding when the agency intends to regulate products as either "drugs" or medical "devices."

FDA states that the impetus for its proposed regulations is a desire to provide guidance regarding the regulatory status of products made or derived from tobacco. However, rather than addressing FDA's regulation of tobacco products, WLF focuses these comments on the proposed changes to two existing regulations, 21 C.F.R. §§ 201.128 and 801.4, which define the terms "intended uses" as applied to drugs and medical devices. As FDA's summary of its proposed regulations points out, the phrase "intended uses" is relevant to products made or derived from tobacco products, because such products are subject to FDA regulation as "drugs" or "devices" if they have drug or device "intended uses"—*e.g.*, a tobacco product marketed as a means of reducing weight. Nonetheless, the definition of "intended uses" arises much more frequently in the context of products already approved by FDA for marketing as drugs or devices. If such

products are regularly prescribed by physicians for off-label uses, a critically important regulatory issue routinely arises: should the manufacturer be deemed to have "intended" those off-label uses?

FDA states that it is "taking the opportunity to propose" changes to the two "intended uses" regulations (one covering drugs, the other covering devices) in order "to conform them to how the Agency currently applies these regulations to drugs and devices generally." 80 Fed. Reg. at 57756. WLF respectfully submits that the proposed revisions do not adequately reflect recent First Amendment case law, which has significantly curtailed FDA authority to ascribe to a manufacturer an intent to engage in off-label distribution and sales based on truthful statements regarding its product's qualities.

In particular, WLF urges FDA to revise Proposed §§ 201.128 and 801.4 to state explicitly that: (1) FDA recognizes manufacturers' First Amendment right to speak truthfully about their products in appropriate settings without fear that such statements will be used to create new "intended uses" for their products; (2) in determining intent, FDA will focus principally on language contained either on the product label or on immediately accompanying material—and to a lesser extent on language contained in widely circulated advertising material; (3) isolated truthful statements by manufacturers or their representatives will not by themselves be sufficient to create an intended use; (4) a manufacturer's knowledge that its product is regularly being offered and used by others for a purpose for which it is neither advertised nor labeled will *never* be deemed evidence that the manufacturer intends such use; and (5) in determining intended uses, FDA will abide by restrictions on FDA authority imposed by federal courts in *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012), and similar First Amendment decisions.

I. Interests of WLF

Washington Legal Foundation is a public interest law firm and policy center with supporters in all 50 States. WLF regularly appears before federal and state courts and administrative agencies to promote economic liberty, free enterprise, a limited and accountable government, individual and business civil liberties, and the rule of law. In particular, WLF has devoted substantial resources over the years to promoting the free speech rights of the business community, appearing before numerous federal courts in cases raising commercial free speech and other First Amendment issues. *See, e.g.*, *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653 (2011); *Nike v. Kasky*, 539 U.S. 654 (2003). WLF has successfully challenged the constitutionality of FDA restrictions on speech by pharmaceutical manufacturers. *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998), *appeal dism'd*, 202 F.3d 331 (D.C. Cir. 2000). As a result of that litigation, FDA is subject to a permanent injunction limiting FDA's authority to suppress dissemination of certain journal articles/medical texts by manufacturers discussing off-label uses of their FDA-approved products. More recently, WLF lawyers played a key role in overturning—on First Amendment grounds—the criminal conviction of a pharmaceutical representative for conspiring to violate the Federal Food, Drug, and Cosmetic Act (FDCA); the representative's alleged "crime" consisted of speaking truthfully about off-label uses of a drug manufactured by his company. *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012).

WLF also regularly participates in FDA administrative proceedings in support of expanded First Amendment rights. *See, e.g.*, FDA Docket No. FDA-2008-D-0053 (May 15, 2014) (response to revised FDA Draft Guidance on distributing scientific and medical publications on off-label uses); FDA Docket No. FDA-2013-N-1430 (April 14, 2014) (response to FDA Draft Guidance on postmarket submissions to FDA of interactive promotional media);

FDA Docket No. FDA-2011-D-0868 (March 29, 2012) (response to FDA Draft Guidance on unsolicited requests for off-label information); FDA Docket No. FDA-2008-D-0053 (April 21, 2008) (response to FDA Draft Guidance on good reprint practices); FDA Citizen Petition No. 2006P- 0319/CPI (August 11, 2006) (documenting repeated First Amendment violations by FDA's Division of Drug Marketing, Advertising, and Communications (DDMAC) and calling on DDMAC to comply with constitutional constraints on its activities); FDA Docket No. FDA-02N-0209 (October 28, 2002) (response to FDA's request for public comments on First Amendment issues).

II. The FDCA's Definitions of "Drug" and "Device"

A product's intended use is central in determining whether it is a drug or device subject to FDA regulation. The FDCA, 21 U.S.C. § 301 *et seq.*, defines a "drug" as an article *intended* either: (1) for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; or (2) to affect the structure of the body. FDCA § 201(g)(1), 21 U.S.C. § 321(g)(1). The FDCA's definition of a "device" is very similar. FDCA § 201(h), 21 U.S.C. § 321(h). The principal feature that distinguishes these two categories is the presence or absence of a "chemical action"; a product is a device and not a drug if it "does not achieve its primary intended purposes through chemical action within or on the body of man or other animals." FDCA § 201(h)(3), 21 U.S.C. § 321(h)(3).

The FDCA bars the distribution and sale in interstate commerce of any drug or device without FDA approval or clearance. That approval requirement applies to each intended use of a drug or device; a drug may not be sold for a second intended use simply because FDA has approved it for one intended use. FDA's regulatory definition of "intended uses" is thus critically important to all manufacturers, because a manufacturer could face severe civil or

criminal sanctions if FDA determines that the manufacturer intended that one of its products be used for an unapproved medical purpose. For the reasons set forth below, WLF respectfully submits that FDA should significantly contract its proposed definitions of "intended uses." FDA's broad proposed definitions impinge on manufacturer First Amendment rights by threatening severe sanctions for those who disseminate truthful scientific information about off-label uses of their FDA-approved products.

III. The First Amendment Imposes Significant Restrictions on FDA's Authority to Regulate Manufacturer Speech

The federal courts have long recognized that the First Amendment, subject only to narrow and well-understood exceptions, does not countenance governmental control over the content of messages conveyed by private individuals. *See, e.g.*, *Texas v. Johnson*, 491 U.S. 397, 414 (1989). "As a general matter, 'state action to punish the publication of truthful information can seldom satisfy constitutional standards.'" *Barnicki v. Vopper*, 532 U.S. 514, 527 (2001) (quoting *Smith v. Daily Mail Publishing Co.*, 443 U.S. 97, 102 (1979)). The heavy burden of justifying content-based restrictions speech rests on the government. *R.A.V. v. St. Paul*, 505 U.S. 377, 382 (1992) ("Content-based regulations are presumptively invalid," and the government bears the burden to rebut that presumption.).

"Speech in the aid of pharmaceutical marketing . . . is a form of expression protected by the . . . First Amendment . . . ." *Sorrell*, 131 S. Ct. at 2659. And when regulating purely commercial speech, the government must still "justify its content-based law as consistent with the First Amendment." *See id.* at 2662-64, 2667 (Regulation of speech in pharmaceutical marketing was "presumptively invalid" and the "outcome [was] the same whether a special commercial speech inquiry or a stricter form of judicial scrutiny applied."). "The government

cannot 'completely suppress information when narrower restrictions on expression would serve its interests as well.'" *Caronia*, 703 F.3d at 164 (quoting *Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of New York*, 447 U.S. 557, 565 (1980)). This is because "bans against truthful, nonmisleading commercial speech . . . usually rest solely on the offensive assumption that the public will respond 'irrationally' to the truth . . . ." *Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 503 (1996).

"The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good." *Ibid.* So when regulating non-misleading speech that concerns lawful activity, the government must prove that its regulation is "narrowly drawn" and advances a substantial government interest "to a material degree." *Id.* at 505; *Central Hudson*, 447 U.S.at 565-66.

IV. Federal Courts Have Repeatedly Blocked FDA Efforts to Restrict Speech that Arguably Demonstrates an Intent to Sell a Product for an Off-Label Use

Over the past several decades, federal courts have repeatedly held that FDA's restrictions on manufacturer speech are subject to significant First Amendment constraints and have held on numerous occasions that FDA speech restrictions were constitutionally impermissible. *See, e.g.*, *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012); *Thompson v. Western States Med. Ctr.*, 535 U.S. 357 (2002); *Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999); *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998), *appeal dism'd*, 202 F.3d 331 (D.C. Cir. 2000). Given this history, it is disappointing that FDA would amend 21 C.F.R. §§ 201.128 and 801.4 for the first time in nearly 40 years, but fail to write those regulations in a manner clarifying that FDA recognizes and respects that the First Amendment protects truthful commercial speech.

The breadth of FDA's proposed definition of "intended uses" has consequences that vary by the particular type of speech it seeks to regulate. Insofar as FDA applies this definition to the regulation on non-commercial speech, the agency cannot plausibly argue that its regulation could pass constitutional muster. Accordingly, any speech regulation by FDA must be limited to commercial speech. Yet, there are certainly instances where an employee or representative of a drug manufacturer may disseminate truthful information in a noncommercial manner—for example dissemination of peer-reviewed journal articles.

FDA officials must come to grips with Supreme Court case law limiting the definition of commercial speech to that which "does no more than propose a commercial transaction." *Bolger v. Youngs Products Corp.*, 463 U.S. 60, 66 (1983). While some communication by employees or other individuals acting on a manufacturer's behalf may be in the furtherance of a proposed commercial transaction, not all exchanges of information fit this criterion. The mere existence of an underlying profit-making motivation does not transform noncommercial speech into commercial speech. *See Bd. of Trustees of State University of New York v. Fox*, 492 U.S. 469, 482 (1989) ("Some of our most valued forms of fully protected speech are uttered for a profit.").

Moreover, even manufacturer speech that is truly commercial in nature is still entitled to considerable constitutional protection, and it is incumbent on FDA to tailor its regulatory scheme to respect First Amendment boundaries. FDA's proposed regulations do not exhibit such tailoring. FDA's "construction of the FDCA's misbranding provisions to prohibit and criminalize off-label promotion is content- and speaker-based, and subject to heightened scrutiny under *Sorrell*," *Caronia*, 703 F.3d at 165, yet FDA continues to ignore the import of these decisions and proposes regulations that continue to disregard the First Amendment. 80 Fed. Reg. 57761 (FDA's proposed Amendments "[do] not reflect a change in FDA's approach regarding evidence

of intended use for drugs and devices."). By threatening to rely on any and all truthful manufacturer speech as evidence of intent to market a product for an unapproved new medical use, FDA runs afoul of the First Amendment.

As noted above, the *Central Hudson* test provides that government regulation of truthful speech concerning a lawful activity violates the First Amendment unless government regulators can establish that: (1) they have identified a substantial government interest; (2) the regulation "directly advances" that asserted interest; and (3) the regulation "is no more extensive than is necessary to serve that interest." *Central Hudson*, 447 U.S. at 566. A complete prohibition of truthful speech by manufacturers and their representatives concerning the off-label uses of a drug or device cannot satisfy this strict standard and, as such, is an unconstitutional restraint on free speech. *See, e.g.*, *Caronia*, 703 F.3d at 166-67 ("As off-label drug use itself is not prohibited, it does not follow that prohibiting the truthful promotion of off-label drug usage by a particular class of speakers would directly further the government's goals of preserving the efficacy and integrity of FDA's drug approval process and reducing patient exposure to unsafe and ineffective drugs. . . . [Nor does] criminalizing manufacturer promotion of off-label use while permitting others to promote such use to physicians . . . directly advance [the FDCA's] interests . . . .").

FDA's refusal to consider the constitutional bounds of its authority in the drafting of its regulations will have a chilling effect on legally protected speech. And "in the fields of medicine and public health, 'where information can save lives,' it only furthers the public interest to ensure that decisions about the use of prescription drugs, including off-label usage, are intelligent and well informed." *Id.* (quoting *Sorrell*, 131 S. Ct. at 2664). Thus, any revision to §§ 201.128 and 801.4 should reflect manufacturers' First Amendment right to speak truthfully about their

products in appropriate settings without fear that such statements will be used to create new "intended uses" for the products.

V. FDA Should Revise its Proposed Regulation to Reflect the Limits on its Authority Imposed by the First Amendment and its Governing Statute

FDA prohibits the "misbranding of any . . . drug [or] device . . . in interstate commerce," with a drug or device considered misbranded if its labeling does not bear "adequate directions for use." 21 U.S.C. §§ 331, 352. FDA has interpreted this governing statute to permit its regulation of all manufacturer speech concerning off-label uses. *See* 21 C.F.R. §§ 201.5 and 801.4. "The consequences for misbranding are criminal." *Caronia*, 703 F.3d at 154 (citing 21 U.S.C. § 333(a)(2)).

While FDA generally does not regulate a physician's off-label prescribing of an approved drug, and has recognized the propriety and potential value of such uses, *see Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 350 (2001), the government has prosecuted manufacturers for misbranding based on their representatives' promotion of a drug or device's off-label uses. *See Caronia*, 703 F.3d at 154 (collecting cases). The proposed regulations go even further, threatening to base "intended use" findings on mere knowledge that *others* are using the drug or device off-label. 21 C.F.R. §§ 201.128 and 801.4. In other words, FDA's proposed regulations permit manufacturer liability for misbranding based on little more than its mere knowledge that a product is being prescribed for an off-label use.[1]

[1] In an apparent effort to soften the proposed regulations' "mere knowledge" language, FDA states in its "Background" material, "As FDA has previously stated, however, the Agency would not regard a firm as intending an unapproved new use for an approved or cleared medical product based *solely* on the firm's knowledge that such product was being prescribed or used by doctors for such use." 80 Fed. Reg. at 57757 (emphasis added). But that assurance is cold comfort to manufacturers, particularly given FDA's inclusion of the word "solely." The FDCA requires "intent," not mere knowledge. 21 U.S.C. § 321(g)(1). Accordingly, the regulation should make clear that manufacturer knowledge of off-label use by others will *never* be used as evidence of a manufacturer's intent.

The U.S. Court of Appeals for the Second Circuit recently cast doubt on the permissibility of FDA's attempts "to prove intended use by reference to promotional statements made by drug manufacturers or their representatives." *Caronia*, 703 F.3d at 162 n.9 ("[I]t still remains unclear how the government would identify criminal misbranding from communications between drug manufacturers and physicians authorized to prescribe drugs for off-label use."). The court explained that this interpretation would lead to nonsensical results, such as allowing for the successful prosecution of a manufacturer shipping its product to a physician who placed an order with the stated intent of prescribing the drug for an off-label use, but not for the same shipment if the doctor never revealed the intended eventual off-label use. *See ibid.* This illustration demonstrates how untenable it is for FDA to equate knowledge with intent.

Moreover, isolated statements by a manufacturer's representative to a physician should never, alone, establish evidence of a drug or device's intended use. *See Caronia*, 703 F.3d at 168. Instead, FDA should determine intent based principally on a manufacturer's volitional speech such as the language contained either on the product label or immediately accompanying material—and to a lesser extent on language contained in widely circulated advertising material.

WLF proposes that FDA revise its proposed regulations by removing entirely the following sentence: "It may be shown, for example, by circumstances in which the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised." 21 C.F.R. §§ 201.128 and 801.4. WLF further suggests that FDA revise its proposed regulations by adding the following statements: (1) FDA recognizes manufacturers' First Amendment right to speak truthfully about their products in appropriate settings without fear that such statements will be used to create new "intended uses" for the products; (2) in determining intent, FDA will focus principally on language contained

either on the product label or on immediately accompanying material—and to a lesser extent on language contained in widely circulated advertising material; (3) isolated truthful statements by manufacturers or their representatives will not by themselves be sufficient to create and intended use; and (4) in determining intended uses, FDA will abide by restrictions on FDA authority imposed by federal courts in *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012), and similar First Amendment decisions.

VI. Conclusion

WLF respectfully requests that FDA revise its proposed regulations in the manner described herein, in order to bring it into compliance with First Amendment and statutory limitations.

Sincerely,

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