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"; Proposed Partial Delay of Effective Date

IN RESPONSE TO THE PUBLIC NOTICE PUBLISHED
AT 83 FED. REG. 2092 (Jan. 16, 2018)

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Submitted Electronically (www.regulations.gov)
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane Room 1061
Rockville, MD 20852

Re: Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses"; Proposed Partial Delay of Effective Date Docket No. FDA-2015-N-2002, 83 Fed. Reg. 2092 (Jan. 16, 2018)

Dear Sir/Madam:

Washington Legal Foundation (WLF) is pleased to have the opportunity to respond to the Food and Drug Administration's (FDA) proposal to indefinitely delay the effective date of the amendments to the existing medical product "intended use" regulations, 21 C.F.R. §§ 201.128 and 801.4, contained in a Final Rule published in the Federal Register dated January 9, 2017.

WLF supports FDA's proposed indefinite delay, in light of our past comments regarding FDA's changes to the definition of "intended use," as applied to drugs and medical devices. WLF filed comments in November 2015 on the proposed "intended use" rule published in the Federal Register on September 25, 2015. WLF's comments were generally supportive of the Proposed Rule; however, we urged the FDA to take additional steps to protect the First Amendment rights of manufacturers to speak truthfully about off-label use of their FDA-approved medical products. WLF was then disappointed with the January 9, 2017 Final Rule, which we viewed as a retreat from the positive aspects of the Proposed Rule. WLF later expressed its support of FDA's decision to delay the effective date of the Final Rule until March

19, 2018 and explained why the Final Rule was both constitutionally and statutorily defective. *See* WLF's comments filed with FDA on May 19, 2017. Due to our substantive and procedural concerns with the Final Rule, WLF supports FDA's proposal to indefinitely delay the effective date of the Final Rule, so that previous concerns raised during the comment period may be fully considered.

WLF's concerns with the Final rule are twofold. The Final Rule was not adopted in compliance with procedures required by the Administrative Procedure Act (APA) because the Proposed Rule failed to provide notice sufficient to alert interested parties regarding the regulation to be adopted. The Final Rule announced an entirely new standard, the "totality of the evidence" standard for determining the "intended use" of a drug or medical device. The totality-of-the-evidence standard is not a "logical outgrowth" of anything FDA has said previously, and nothing in the Proposed Rule provided interested parties with any indication that FDA was contemplating adoption of that standard. The Final Rule is also unconstitutional. As explained in WLF's November 24, 2015 comments, the First Amendment provides significant protection to manufacturers that seek to speak truthfully about off-label uses of their FDA-approved products. By asserting the right to use all such speech as evidence of intended uses – particularly where such evidence may constitute proof of criminal misconduct – the Final Rule runs afoul of the First Amendment. Given these concerns with the Final Rule, WLF supports the indefinite delay of its effective date, so that the concerns raised during the previous comment period may be considered further.

I. Interests of WLF

Washington Legal Foundation is a public-interest law and policy center with supporters nationwide. 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 free-speech rights of consumers and merchants in the marketplace, appearing before numerous federal courts in cases raising First Amendment issues. *See, e.g., Sorrell v. IMS Health Inc*., 564 U.S. 552 (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 authority to suppress manufacturer dissemination of certain journal articles/medical texts discussing off-label uses of their FDA-approved products. More recently, WLF played a key role in overturning on First Amendment grounds the criminal conviction of a pharmaceutical representative for conspiring to violate the FDCA; the representative's 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 appears in court proceedings to ensure that FDA and other federal agencies adhere to the procedural requirements of the APA. *See, e.g., Prevor v. FDA*, 67 F. Supp. 3d 125 (D.D.C. 2014).

WLF also regularly participates in FDA administrative proceedings in support of expanded First Amendment rights. *See, e.g.*, FDA Docket No. FDA-2016-N-1149 (January 3,

2017) (response to FDA request for comments on manufacturer off-label communications); 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 inter-active 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. 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 conform to constitutional constraints on its activities); FDA Docket No. 02N-0209 (October 28, 2002) (response to FDA's request for public comments on First Amendment issues). As noted above, WLF also filed comments in this docket in November 2015 in connection with the Proposed Rule, and again in May 2017 in response to FDA's request for comments on the Final Rule.

II. *The Final Rule Flunks the APA's Logical Outgrowth Requirement*

WLF briefly summarizes the reasons, explained more fully in its May 2017 comments, why FDA's January 2017 adoption of the Final Rule did not comply with the APA's procedural requirements. Postponement of the Final Rule's effective date is thus mandated without regard to the substance of the rule – in order to provide FDA an opportunity to bring itself into compliance with the APA.

A federal agency may not adopt a substantive regulation without first providing interested parties with notice of the regulation, 5 U.S.C. § 553(b), and a meaningful opportunity to participate in the rulemaking through submissions of written data, views, or arguments. 5 U.S.C. § 553(c). Federal appeals courts have concluded that the APA's notice-and-comment requirements are intended to achieve three distinct purposes:

> (1) to ensure that agency regulations are tested via exposure to diverse public comment, (2) to ensure fairness to affected parties, and (3) to give affected parties an opportunity to develop evidence in the record to support their objections to the rule and thereby enhance the quality of judicial review.

Miami-Dade County v. EPA, 529 F.3d 1049, 1058 (11th Cir. 2008); *Council Tree Communications, Inc. v. FCC*, 619 F.3d 235, 250 (3d Cir. 2010).

When an agency's final rule is substantially different from its proposed rule, those purposes are undercut. The final rule will not be tested via exposure to diverse public comment if the final rule was not fairly encompassed within the proposed rule on which the public commented. The parties affected are deprived assurances of fairness when the proposed rule does not provide those parties with fair warning regarding the actual provisions of the final rule. Finally, the affected parties will not have an opportunity to develop evidence in the record to support their objections to the rule and thereby enhance the quality of judicial review if they object to the provisions in the final rule that the proposed rule did not include. The Final Rule adopted by FDA in January 2017 differed substantially from the 2015 Proposed Rule and thereby violated 5 U.S.C. § 553(b) & (c).

The Final Rule adopted by FDA in January 2017 reinstated language that the Proposed Rule had proposed to remove from the prior regulation, and also added an

entirely new standard. The Final Rule reinstated a revised version of a sentence that manufacturers had worried would require them to seek supplemental approval from FDA for a new product use whenever they became aware that doctors were prescribing one of their FDA-approved products for an unapproved use, even when they had done nothing to encourage the use. In a surprise switcheroo, the Final Rule reinstated the sentence in question, in a slightly different form. Even more disturbingly however, the revised sentence adopted an entirely new totality-of-the-evidence standard that signals to manufacturers that FDA claims authority to rely on *any* evidence it deems relevant to intended use, including, as pertinent here, manufacturers knowledge of off-label use by others. This new standard made clear that the FDA claims authority to make "intended use" determinations based not merely on what a manufacturer actually says about its products uses but also on any other evidence that it deems relevant to determining intent.

While agencies are entitled to make *some* changes to proposed rules without re-opening the comment period (*Assoc. of Battery Recyclers, Inc. v. EPA*, 208 F.3d 1047, 1058 (D.C. Cir. 2000)), the APA notice requirement limits such changes by requiring that any final rule adopted by an agency must be a "logical outgrowth" of the rule proposed. *Long Island Care at Home, Ltd. v. Coke*, 551 U.S. 158, 174 (2007). The totality-of-the evidence standard included in the Final Rule does not satisfy the "logical outgrowth" requirement because nothing in the Proposed Rule alerted affected parties that FDA was contemplating adopting that standard in its final rule.

There is no basis for FDA's contention that the totality-of-the-evidence standard represents no change in longstanding agency policy, and thus that the standard is

sufficient to satisfy the "logical outgrowth" test. FDA has been unable to point to *any* occasion prior to issuance of the Final Rule on which it articulated a totality-of-the-evidence standard. Certainly, nothing in the Proposed Rule itself placed interested parties on notice that FDA was contemplating adoption of a totality-of-the-evidence standard. While they would have understood that there was a possibility that FDA would ultimately reject the Proposed Rule and leave the intended-use regulations unchanged, the standard adopted in the Final Rule represents a significant (and unanticipated) change from the *status quo ante*.

III. *The First Amendment Protects Truthful Manufacturer Speech About Off-Label Uses of FDA-Approved Products*

In our previous comments, WLF has repeatedly expressed concerns over the First Amendment issues implicated by both the Proposed Rule and the Final Rule. Over the past several decades, federal courts have repeatedly held that the FDA's restrictions on manufacturer speech are subject to significant First Amendment constraints and that those speech restrictions are 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); *Amarin Pharma, Inc. v. FDA*, 119 F. Supp. 3d 196 (S.D.N.Y. 2015); *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 noted in WLF's previous comments, *Central Hudson* 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 Gas & Elec. Corp. v. Pub. Serv. Comm'n of New York*, 447 U.S. 557, 566 (1980). 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* 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 . . . .").

With such case law in mind, WLF's November 2015 comments urged FDA to amend the Proposed Rule in order to clarify that FDA recognizes that the First Amendment Protects commercial speech. WLF made a number of recommendations for statements FDA could add to "intended use" regulations in order to do so. These recommendations were not added to the Final Rule, and FDA responded (in the preamble to the Final Rule) to several of WLF's First Amendment arguments. In the preamble, FDA questioned the continued vitality of *Caronia*. But as WLF pointed out in its May 2017 comments, the United States never sought review of the Second Circuit's decision, and therefore the Executive Branch was in no position to second-guess the Second Circuit's First Amendment analysis. FDA also cited a Supreme Court decision for the proposition that "content-based restrictions on protected expression are sometimes permissible, and that principle applies to commercial speech." 82 Fed. Reg. at 2211 (citing

Sorrell v. IMS Health Inc., 564 U.S. 552, 579 (2011)). FDA was no doubt correct that speech restrictions imposed on drug and device manufacturers are "sometimes permissible." But as WLF pointed out, FDA bears a heavy burden when it seeks to impose such restrictions on truthful manufacturer speech, and it failed to acknowledge that courts have repeatedly invoked the First Amendment to strike down FDA speech restrictions of that nature.

The Final Rule failed to account for such First Amendment concerns. WLF therefore supports the indefinite delay of the Final Rule's effective date, so that it may be brought in line with recent First Amendment case law.

IV. *An Indefinite Delay of the Effective Date is Justified Under 21 C.F.R. § 10.35(a)*

FDA's proposal to indefinitely delay the effective date of the Final Rule complies fully with APA requirements. WLF believes this is the best course of action in order to allow concerns expressed during the previous comment periods to be fully considered. WLF believes that FDA is completely within its authority under 21 C.F.R. § 10.35(a), which grants the Commissioner the authority to "at any time stay or extend the effective date of an action pending or following a decision on any matter." Additionally, under 21 C.F.R. 10.40(b)(2), the Commissioner may, for "good cause," shorten the comment period for the proposal . Given that FDA provided well over the minimum requirement of 10 days for public comment, and that the Final Rule's current effective date (March 19, 2018) makes a full 60-day comment period impractical, WLF believes the Commissioner has satisfied the good-cause requirement.

WLF also believes that the decision to delay the effective date would withstand any court challenge. The APA imposes a very high burden of proof on any would-be plaintiff who seeks to challenge the delay decision. In order to state a claim against FDA that the agency "unreasonably delayed" enforcement of a regulation, 5 U.S.C. § 706, a plaintiff would have to first show that FDA was required to take action at all. In *Norton v. S. Utah Wilderness All.*, the Supreme Court held that "a delay cannot be unreasonable with respect to action that is not required." 542 U.S. 55, 63 (2004). Therefore, "a plaintiff who asks a court to 'compel agency action … unreasonably delayed' under § 706(1) must pinpoint an agency's failure to take action that it both discrete *and* mandatory." *Center for Biological Diversity v. Zinke*, 260 F. Supp. 3d 11 (D.D.C. 2017) (quoting *Norton v. S. Utah Wilderness All.*, 542 U.S. at 64). It is never "mandatory" for an agency to enforce a regulation whose adoption violated both the APA and the First Amendment. Given the standard of review established by § 706, FDA is acting well within its delegated authority to indefinitely delay the effective date of the Final Rule; it has followed proper procedures under 21 C.F.R. § 10.35(a), and was not required to take action when it has concluded in good faith that additional time is required to fully consider all of the comments received during the previous comment periods.

V. *Conclusion*

WLF fully endorses FDA's decision to indefinitely delay the effective date of the amendments to the existing medical product "intended use" regulations, 21 C.F.R. §§ 201.128 and 801.4.

Sincerely,

/s/ Richard A. Samp_____
Richard A. Samp
Chief Counsel

/s/ Taylor E. Alexander
Taylor E. Alexander
Law Clerk