United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued January 10, 2000 Decided February 11, 2000

No. 99-5304

Washington Legal Foundation,
Appellee

v.

Jane E. Henney, Commissioner,
Food and Drug Administration, and
Donna E. Shalala, Secretary,
U.S. Department of Health and
Human Services, Appellants

Appeal from the United States District Court
for the District of Columbia
(No. 94cv01306)

William B. Schultz, Deputy Assistant Attorney General, United States Department of Justice, argued the cause for appellants. With him on the briefs were David W. Ogden, Acting Assistant Attorney General, Douglas N. Letter and

Michael S. Raab, Attorneys, Wilma A. Lewis, United States Attorney, Eric M. Blumberg, Deputy Chief Counsel for Litigation, Food and Drug Administration, and Annamarie Kempic, Associate Chief Counsel for Enforcement.

Bert W. Rein argued the cause for appellee. With him on the brief were Daniel J. Popeo, Richard A. Samp, Andrew S. Krulwich, Thomas W. Queen, Daniel E. Troy, and Michael L. Sturm.

Matthew Van Hook, Peter Barton Hutt, Bruce N. Kuhlik, and Michael S. Labson were on the brief for amicus curiae Pharmaceutical Research and Manufacturers of America.

Arthur B. Spitzer and Daniel I. Prywes were on the brief for amicus curiae American Civil Liberties Union of the National Capital Area.

Before: Silberman, Williams, and Tatel, Circuit Judges.

Opinion for the Court filed by Circuit Judge Silberman.

Silberman, Circuit Judge: The government appeals a district court decision holding that the Food and Drug Administration Modernization Act of 1997, which establishes procedures by which drug and medical device manufacturers may disseminate information about "off-label" uses for their products, violates the First Amendment. In light of the government's appellate position that the statute does not provide it with independent authority to proscribe speech, we dismiss the appeal and vacate the district court's injunction.

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To secure Food and Drug Administration (FDA) approval for a drug or medical device,1 a manufacturer must demonstrate that its product is safe and effective for each of its intended uses. See 21 U.S.C. s 355(d); id. at s 360e(e)(1)(A). It will often be discovered after initial FDA approval, however, that a drug has uses other than those for which it was

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1 For brevity's sake we use the term "drugs" to encompass drugs and medical devices, both of which are regulated under the statute and guidance document at issue here.

approved. These so-called "off-label uses" are subject to asymmetrical--if not necessarily inconsistent--regulatory treatment. On the one hand, it is unlawful for a manufacturer to introduce a drug into interstate commerce with an intent that it be used for an off-label purpose, see id. at s 331(d), and a manufacturer illegally "misbrands" a drug if the drug's labeling includes information about its unapproved uses, see id. at s 331(a); id at s 352(a); cf. Kordel v. United States, 335 U.S. 345, 348-50 (1948) (affirming broad definition of "labeling" under the Food, Drug, and Cosmetic Act). On the other hand, neither Congress nor the FDA has attempted to regulate the off-label use of drugs by doctors and consumers. A physician may prescribe a legal drug to serve any purpose that he or she deems appropriate, regardless of whether the drug has been approved for that use by the FDA. See, e.g.,

Citizen Petition Regarding the Food and Drug Administration's Policy on Promotion of Unapproved Drugs and Devices; Request for Comments, 59 Fed. Reg. 59,820, 59,821 (1994). Although the parties have differing views about the health risks and benefits of off-label uses, it is undisputed that the prescription of drugs for unapproved uses is commonplace in modern medical practice and ubiquitous in certain specialties. See, e.g., James M. Beck & Elizabeth D. Azari, FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions, 53 Food & Drug L.J. 71, 80 (1998).

While a manufacturer's direct advertising or explicit promotion of a product's off-label uses is likely to provoke an FDA misbranding or "intended use" enforcement action, manufacturers have sought to employ more indirect methods of informing physicians about their products' off-label uses. This case concerns the FDA's and Congress' attempts to regulate two of these promotional strategies: manufacturer dissemination to physicians of independent medical and scientific publications concerning the off-label uses of their products, and manufacturer support for Continuing Medical Education (CME) programs for doctors that focus on off-label uses. The FDA's examination of these practices led to publication of an agency enforcement policy set forth in three

guidance documents. Two of these documents limited the circumstances under which manufacturers could permissibly distribute "enduring materials"--i.e., journal article reprints and textbooks--to physicians. See Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data and Guidance for Industry Funded Dissemination of Reference Texts, 61 Fed. Reg. 52,800 (1996) ("Enduring Materials Guidances").2 The third guidance document, concerning manufacturer involvement in CME programs (the "CME Guidance"), set forth twelve factors that the FDA will consider in determining whether a program is independent of manufacturer influence. See Guidance for Industry: Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64,093, 64,096-99 (1997).

Washington Legal Foundation (WLF) brought this action asserting that the policies articulated in the Guidance Documents violated the First Amendment right of its physician members to receive information about off-label uses from manufacturers.3 Cf. Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc., 425 U.S. 748, 756-57 (1976) (First Amendment protections extend both to distribution and receipt of commercial speech). The district court, in its decision granting summary judgment, began its discussion

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2 These Guidances provided that, while a manufacturer-distributed article could reference a product's off-label use, "the principal subject of the article should be the use[ ] ... that has been approved by FDA," 61 Fed. Reg. at 52,801; it also stated that the manufacturer should indicate clearly to the recipient that the article discusses "information that is different from approved labeling." Id. The Guidances included similar provisions limiting the dissemination of medical textbooks where the textbook contains content too extensively devoted to off-label uses. See id.

3 WLF's original complaint, filed before the FDA published the Guidances, was based on a series of FDA actions taken against manufacturers for their dissemination of off-label information that WLF asserted constituted final agency policy. See Washington Legal Foundation v. Kessler, 880 F.Supp. 26 (D.D.C. 1995). The Guidance Documents were published during the course of the litigation.

of WLF's constitutional claim by classifying the speech being regulated. Rejecting both the WLF's contention that the policies restricted fully-protected scientific speech and the FDA's argument that the speech was constitutionally unprotected because it "proposed an illegal transaction," the court determined that the Guidance Documents regulated commercial speech. See Washington Legal Foundation v. Friedman, 13 F.Supp.2d 51, 62-65 (D.D.C. 1998) (WLF I). It then applied the three-part test set forth in Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n, 447 U.S. 557 (1980), to determine whether the policies' restrictions on commercial speech exceeded constitutional limits. It concluded that the Guidance Documents satisfied the first and second parts of Central Hudson, since they directly advanced the government's substantial interest in encouraging manufacturers to seek FDA approval for off-label uses. They fell short of satisfying the final part of the Central Hudson test, however, because the policies restricted considerably more speech than necessary to encourage manufacturers to achieve this objective. See WLF I, 13 F.Supp.2d at 65-74. Holding that the Enduring Materials and CME Guidances violated the First Amendment, the court enjoined the FDA from prohibiting manufacturers' dissemination of enduring materials "regardless of whether such [materials] include[ ] a significant or exclusive focus" on off-label uses, and from proscribing manufacturers from suggesting content to CME program providers. Id. at 74-75.

Shortly after the district court issued its injunction, the Food and Drug Administration (FDA) Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (FDAMA or the Act), became effective. The Act includes provisions concerning manufacturer distribution of enduring materials on off-label uses that supersede4 the Enduring Materials Guidances

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4 We emphasize that the FDA unequivocally stipulated in its briefs and at oral argument that the Act and its implementing regulations supersede, rather than supplement, the Enduring Material Guidances. And even if they were not superseded, they would be unenforceable, since the FDA does not challenge on appeal the

found unconstitutional in WLF I. See 21 U.S.C. ss 360aaa et seq. It specifically authorizes a manufacturer to disseminate "written information concerning the safety, effectiveness, or benefit of a use not described in the approved labeling of a drug or device," 21 U.S.C. s 360aaa(a), if it complies with several requirements: the manufacturer must submit an application to the FDA seeking approval of the drug for the off-label use; the manufacturer must provide the materials to the FDA prior to dissemination; the materials themselves must be in unabridged form; and the manufacturer must include disclosures that the materials pertain to an unapproved use of the drug, and, if the FDA deems it appropriate, "additional objective and scientifically sound information ... necessary to provide objectivity and balance." See 21 U.S.C. s 360aaa(b)(1)-(6); id. at 360aaa(c); id. at 360aaa-1. Importantly, the Act amends the Food, Drug, and Cosmetic Act to prohibit "[t]he dissemination of information in violation" of these provisions. 21 U.S.C. s 331(z); see also id. at s 360aaa-4(b)(1) (emphasis added).

After the Act became effective, questions arose concerning the scope of the district court's decision and injunction in WLF I. The government asserted that the district court's ruling applied only to the Guidance Documents, two of which had been superseded by the Act, and asked that the district court confine the application of its injunction accordingly. The court denied the FDA's motion, noting that its "decision and injunction must be read to apply to the underlying policies of the FDA, and not merely to the express provisions of the Guidance Documents," Washington Legal Foundation v. Friedman, 36 F.Supp.2d 16, 18 (D.D.C. 1999) (WLF II), and requested supplemental briefing on the constitutionality of the Act's provisions addressing manufacturer promotion of off-label uses. In a subsequent opinion, the district court held that those provisions, like the Enduring Materials Guidances that preceded them, violated the First Amendment. See Washington Legal Foundation v. Henney, 56 F.Supp.2d

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district court's decision and injunction insofar as they pertain to the Enduring Material Guidances. See WLF I, 13 F.Supp.2d at 74.

81 (D.D.C. 1999) (WLF III). The FDA appealed, contending that the district court erred in concluding that the FDAMA and the CME Guidance are unconstitutional.

The stage therefore appeared set for us to consider a difficult constitutional question of considerable practical importance. However, as a result of the government's clarification at oral argument, the dispute between the parties has disappeared before our eyes. The parties' briefs were quite confusing as to the meaning of the Act and the CME Guidance, perhaps because both provisions became effective during the later stages of the litigation in the district court. While WLF clearly understood these provisions as independently banning both manufacturer dissemination of enduring materials on off-label uses and support for CME conferences, see, e.g., Appellee's Br. at 1, 12-13, 20, 33, the FDA's view of the Act and the CME Guidance was somewhat unclear: At times the FDA appeared to share WLF's assessment that these provisions provide legal authorization to restrict manufacturer speech, but more frequently the FDA asserted that they established nothing more than a "safe harbor" ensuring that certain forms of conduct would not be used against manufacturers in misbranding and "intended use" enforcement actions based on pre-existing legislative authority. Compare Appellant's Br. at 34-35 (safe harbor) with id. at 46-47, 51 (describing provisions as restricting speech, and noting that "enforcement of the FDCA's misbranding provision ... is a wholly inadequate substitute for the FDAMA"). In response to questioning at oral argument, the government definitively stated that it subscribed to the "safe harbor" interpretation and further explained that, in its view, neither the FDAMA nor the CME Guidance independently authorizes the FDA to prohibit or to sanction speech.5 When we

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5 The government's position, articulated and repeated several times during oral argument, is most succinctly presented by the following colloquy:

> THE COURT: .... I thought your whole explanation of this statute and the guidance was that they have established a procedure for manufacturers who distribute certain materials

pressed government counsel about the significance of 21 U.S.C. s 331(z)--which specifically prohibits "the dissemination of information in violation of section 360aaa"--he explained that this provision provides that a manufacturer who disregards section 360aaa's conditions cannot avail itself of the FDAMA safe harbor, and might be liable in some fashion if it breached an agreement with the Secretary pursuant to that section. See Tr. at 34. Were a pharmaceutical company to send out reprints of an article devoted to its drug's off-label uses to thousands of physicians tomorrow, the government agreed--indeed stipulated-that the agency would draw no independent prosecutorial authority from FDAMA to buttress any enforcement proceeding. See Tr. at 60--61. And the FDA offers a similar view of the CME Guidance: If a drug manufacturer wishes to suggest content to a CME program provider in a manner that runs afoul of all the Guidance's twelve "factors" that, by itself, is not a violation of law. See Tr. at 73-74. Although the FDA retains the prerogative to use both types of arguably promotional conduct as evidence in a misbranding or "intended use" enforcement action, cf. Action on Smoking and Health v. Harris, 655 F.2d 236, 239 (D.C. Cir. 1980) (observing that "it is well established that the 'intended use' of a product, within the meaning of the [Food, Drug, and Cosmetic] Act, is determined from its label, accompanying labeling, promotional claims, advertising, and any other relevant source" (internal citations omitted)), the agency insists that nothing in either of the provisions challenged in this case provides the FDA with independent authority to regulate manufacturer speech.

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regarding off-label uses in such a way that they will not be used as evidence against them in a prosecution under the misbranding provisions. I thought that's what this was about. And that I thought that any manufacturer could distribute anything they wanted, if they wanted to take a chance of ending up a defendant in a mislabeling case. Isn't that right?

COUNSEL: That's all correct. That's all correct.

THE COURT: That's all correct.

COUNSEL: Yes.

Tr. at 31-32.

WLF responded that in light of the government's position as refined and explained at oral argument it no longer has a constitutional objection to the Act or the CME Guidance,6 see Tr. at 52, 66-68, 69--a response that, it would seem, eliminates entirely the only issues in dispute between the parties in this case. WLF apparently believes we should nevertheless affirm the district court. It is a well-recognized principle that a case will not become moot merely because a defendant agrees voluntarily to cease engaging in the challenged conduct, as there remains a risk that the defendant will merely resume the challenged conduct after the case is dismissed. See, e.g., United States v. W. T. Grant Co., 345 U.S. 629, 632 (1953). Voluntary cessation of challenged conduct will only moot a case if "subsequent events made it absolutely clear that the allegedly wrongful behavior could not reasonably be expected

to recur." Friends of the Earth, Inc. v. Laidlaw Environmental Servs. (TOC), Inc., No. 98-222, Slip Op. at 18 (U.S. Jan. 12, 2000) (quoting United States v. Concentrated Phosphate Export Assn., Inc., 393 U.S. 199, 203 (1968)). Relying on this principle, and apparently concerned that the FDA will prosecute manufacturers for violating a normative standard set forth in the Act or CME Guidance notwithstanding the agency's concession in this case that it has no authority to do so, WLF indicates that we should still reach the merits of the district court's decision and injunction.

We think that WLF misapprehends the nature and significance of the FDA's concessions, which do not in our view implicate principles of mootness at all. This is not an instance of "voluntary cessation," since WLF has not alleged that FDA engaged in any conduct pursuant to the challenged statute and guidance document. The relevant question before us therefore is not whether certain enforcement activities conducted under these provisions were unconstitutional (since there were no such activities alleged), but instead whether the statute and guidance document facially violate the First

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6 A manufacturer, of course, may still argue that the FDA's use of a manufacturer's promotion of off-label uses as evidence in a particular enforcement action violates the First Amendment.

Amendment. Since both parties now agree that they do not, there is no constitutional controversy between the parties that remains to be resolved; we do not think it at all appropriate to rule on the constitutionality of a hypothetical interpretation of a statute, see Aetna Life Ins. Co. v. Haworth, 300 U.S. 227, 240-41 (1937) (distinguishing a justiciable controversy from "a difference or dispute of a hypothetical or abstract character"), which is what WLF in effect requests by suggesting that we "reach the merits" of the district court's decision. The government has announced here nothing less than an official interpretation of the FDAMA which the agency may not change unless it provides a reasoned explanation for doing so. See Amax Land Co. v. Quarterman, 181 F.3d 1356, 1365 & n.6 (D.C. Cir. 1999). It goes without saying that an attempt to evade judicial review in this case would hardly be a legitimate basis. Cf. AT & T v. FCC, 978 F.2d 727, 731-32 (1993).

Accordingly, we dismiss the FDA's appeal and vacate the district court's decisions and injunctions insofar as they declare the FDAMA and the CME Guidance unconstitutional.7

So ordered.

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7 In disposing of the case in this manner, we certainly do not criticize the reasoning or conclusions of the district court. As we have made clear, we do not reach the merits of the district court's First Amendment holdings and part of its injunction still stands.