



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

7434 '02 JAN 30 09:52

January 28, 2002

Daniel J. Popeo, Esq.
Richard A. Samp, Esq.
Washington Legal Foundation
2009 Massachusetts Avenue, N.W.
Washington, D.C. 20036

Re: Docket No. 01P-0250

Dear Messrs. Popeo and Samp:

This letter responds to your citizen petition, filed with the Food and Drug Administration (FDA) on May 29, 2001, on behalf of the Washington Legal Foundation (WLF), and to supporting comments filed on behalf of the Coalition for Healthcare Communication on November 13, 2001. FDA provided an interim response to your petition on November 16, 2001, promising a final response by mid-January, 2002. Your petition asks FDA to "withdraw the Federal Register Notice it published on March 16, 2000, entitled, 'Decision in Washington Legal Foundation v. Henney'" and in its stead to issue a "policy statement indicating [FDA's] adherence to the decision of the U.S. District Court for the District of Columbia in *Washington Legal Foundation v. Friedman*." You allege that the Federal Register notice "violates the First Amendment rights of manufacturers who wish to speak in a non-misleading manner about off-label uses of their products and the rights of WLF, its members, and others who wish to hear such speech." Your petition further requests that FDA ensure that its enforcement personnel are educated about applicable First Amendment law. Finally, you request that FDA issue additional guidance on the agency's enforcement policy regarding manufacturer support of continuing medical education programs (CME).

FDA recognizes that in enforcing the Federal Food, Drug and Cosmetic Act (FDCA) and thereby furthering the Agency's mission to protect the public health, it must respect the rights guaranteed by the First Amendment. Consequently, FDA is working to ensure that its personnel understand that the FDCA does not contain an independent prohibition against the dissemination of truthful, nonmisleading reprints of articles or textbook excerpts regarding unapproved new uses of approved medical products or against manufacturer sponsorship of CME at which such uses will be discussed. Under new FDA policy, agency warning and untitled letters are also reviewed by the FDA Office of Chief Counsel for legal sufficiency, including adherence to the First Amendment, prior to their issuance. Consistent with FDA's position in the prior litigation between the agency and WLF, FDA also instructs personnel that the FDCA, as amended by the Food and Drug Administration Modernization Act of 1997 (FDAMA), provides a specific "safe harbor" for manufacturers that wish to distribute materials regarding unapproved new uses without any risk that this activity may be used as evidence of their intent that the product that they are distributing be used for an unapproved use. As a matter of enforcement discretion,

01P-0250

PDN 1

FDA's current CME guidance also outlines a safe harbor of circumstances under which manufacturer activity will not be considered as potential evidence of intent that a product be used for an unapproved new use. As addressed below, however, FDA remains free on a case-by-case basis to pursue product seizures, injunctions, and other enforcement actions to address substantive violations of section 301 of the Act, using any and all evidence of the manufacturer's intent regarding the use of the product, including evidence of distribution of reprints or sponsorship of CME, where such activity does not conform to the safe harbors described above.¹ In such a case, a manufacturer may raise a First Amendment challenge to FDA's enforcement action, although of course we would fully expect that any such action would be devoid of any First Amendment infirmities.

FDA's activities in this respect are fully consistent with the Federal Register notice of March 16, 2000, with the decision of the United States Court of Appeals for the District of Columbia in Washington Legal Foundation v. Henney, 202 F.3d 331 (D.C. Cir. 2000), and with the positions of both FDA and Washington Legal Foundation in argument before that Court. These activities are not barred by the prior district court decisions regarding FDA's superseded guidance documents addressing reprints of journal articles and textbook excerpts. Consequently, FDA denies your request that it withdraw the Federal Register notice and reinstate the district court injunction vacated by the Court of Appeals decision.

I. The Federal Register notice is consistent with both parties' positions in the Court of Appeals and thus does not present a facial violation of the First Amendment.

The Federal Register notice reiterates that which FDA stated before the D.C. Circuit: The FDCA does not contain an independent prohibition against manufacturers' distribution of truthful, nonmisleading reprints or sponsorship of CME addressing unapproved new uses of the manufacturers' drugs or devices.² See Washington Legal Foundation v. Henney, 202 F.3d at 335

¹ The manufacturer's intent is critical in all cases under the FDCA, for it is by ascertaining the manufacturer's objective intent that FDA establishes not only whether the manufacturer has conformed to the approval requirements of the Act, but even whether the manufacturer's product is a drug or device at all. 21 U.S.C. §§ 321(g) (defining drug in relation to its intended use); 321(h) (defining device in relation to its intended use). And to establish this intent, FDA is entitled to look to a variety of direct and circumstantial evidence from which an objective observer could determine for what use the manufacturer intended its product. See, e.g., 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"); Hanson v. United States, 417 F. Supp. 30, 35 (D. Minn.), aff'd, 540 F.2d 947 (8th Cir. 1976) (same); United States v. Travia, Cr. No. 01-0372-01, (D.D.C., November 30, 2001), Slip Op. at 6-7 (holding that "labeling is not exclusive evidence of the seller's intent," noting that even consumer intent could be relevant evidence of seller's intent, and finding nitrous oxide to be a drug from the circumstances of its sale, even where no labeling or oral statements accompanied product); United States v. Undetermined Quantities of Articles of Drug, 145 F. Supp. 2d 692, 698-99 (D. Md. 2001) (stating that "[o]f primary significance in determining whether a product may be deemed a 'drug' is its intended use or effect as gathered from the objective evidence disseminated by the vendor" and finding product to be drug where, among other things, marketing suggested that product was substitute for illegal drugs); United States v. 250 Jars, Etc. of U.S. Fancy Pure Honey, 218 F. Supp. 208, 211 (E.D. Mich. 1963) ("In determining that a particular article was intended to be used as a drug, a court is not limited to the labels on such article or to the labeling which accompanies it, but may look at all relevant sources."); 21 C.F.R. §§ 201.128 (defining indicia of "intended use" for drugs); 801.4 (defining indicia of "intended use" for devices). Inevitably, much of the evidence of intent is in the form of speech.

² As it did throughout the litigation, FDA continues to state that the CME guidance document merely outlines a safe harbor. This was intended to be the message of the Federal Register notice. See, e.g., 65 FR 14287 (stating that

("In response to questioning at oral argument, the government . . . explained that, in its view, neither the FDAMA nor the CME Guidance independently authorizes FDA to prohibit or sanction speech."); *id.* at 336 ("the agency insists that nothing in either of the provisions challenged in this case provides the FDA with independent authority to regulate manufacturers' speech") (emphasis added); TR³ at 31-32 (cited in WLF v. Henney, 202 F.3d at 335 n.5), TR at 73-74 (addressing CME; cited in WLF v. Henney, 202 F.3d at 336); 65 FR 14287 (March 16, 2000).

What the FDCA does prohibit, however, is introducing or causing the introduction into interstate commerce of a drug or device intended for a use that has not been approved or cleared by FDA,⁴ even if that same product is approved or cleared for a different use.⁵ These substantive restrictions on manufacturer activity are the linchpin of the FDCA and are designed to ensure that the only products that are on the market are ones that have been confirmed by FDA to be safe and effective for each and every use for which they are intended. If a manufacturer of a drug legally marketed for one use were free to market the drug for additional, unapproved uses, that would effectively quash the incentive for the manufacturer to expend the substantial resources necessary to demonstrate safety and effectiveness for the additional uses. To preserve that incentive, the Act prohibits the manufacturer from distributing such an approved drug for such unapproved but intended uses. As interstate distribution is a given for a product approved for at least one purpose, the crucial considerations in enforcing this prohibition necessarily center on any evidence of the manufacturer's intended uses.⁶ In light of the approval requirements of the Act, a manufacturer's activities evidencing an intent for the use of a product that has not been approved for any use are legally indistinguishable from those demonstrating its intent for an

FDA would continue its existing policy toward CME and reiterating that "[i]f a manufacturer does not follow the CME guidance document, that, by itself, is not an independent violation of the law").

³ Cites to TR are to the transcript of oral argument in Washington Legal Foundation v. Henney, No. 99-5304, argued January 10, 2000, before the United States Court of Appeals for the District of Columbia Circuit. A copy of the transcript is on file with FDA's Dockets Management Branch.

⁴ See, e.g., Section 301(a), 21 U.S.C. § 331(a) (prohibiting introduction or delivery for introduction into interstate commerce of any misbranded or adulterated drug or device); Section 502(o), 21 U.S.C. § 352(o) (device is misbranded without a cleared 510(k)); Section 501(f), 21 U.S.C. § 351(f) (class III device is adulterated without approved PMA); Section 502(f), 21 U.S.C. § 352 (f) (drug or device is misbranded unless its label bears adequate directions for intended use); Section 505(a), 21 U.S.C. § 355(a) ("No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug"); Section 301(d), 21 U.S.C. § 331(d) (prohibiting introduction of a product into interstate commerce in violation of 21 U.S.C. § 355(a)). See also 42 U.S.C. § 262(j) (establishing applicability of FDCA to biological products regulated under Public Health Service Act); United States v. Miami Serpentarium Laboratories, [1981-1982 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,164 (S.D. Fla. 1982) (biologics may be regulated as drugs); United States v. Calise, 217 F. Supp. 705, 709 (S.D.N.Y. 1962) (same).

⁵ See, e.g., Washington Legal Foundation v. Friedman, 13 F. Supp. 2d 51, 71 (D.D.C. 1998) ("Congress has declared that *all* uses for a drug must be proved safe and effective by the FDA and has recently reaffirmed that position through the 1997 Food and Drug Amendments"); *id.* at 55 (indicating that Congress has firmly established that each subsequent intended use of a drug must be established to be safe and effective under the same FDA standards and procedures as the initial intended use).

⁶ Where the totality of the evidence is found by the trier of fact to establish a violation, in fashioning remedies, a court would not be limited to stopping the distribution in interstate commerce of the affected medical product, as this would undermine the strong public health interest in maintaining the availability of the product for its approved uses. For example, if an approved cancer therapeutic were established to have been promoted for an unapproved use in cardiovascular disease, the court could remedy the violation by enjoining such promotion rather than removing the product from interstate commerce altogether.

unapproved use of a product already legally marketed for a different use. Thus, FDA can bring actions for alleged violation of these statutory requirements, whether the product is approved for any use or not, relying on proof of distribution of reprints or sponsorship of CME, as well as any other available evidence, to demonstrate the manufacturer's intent. See WLF v. Henney, 202 F.3d at 336 ("FDA retains the prerogative to use both types of arguably promotional conduct as evidence in a misbranding or "intended use" enforcement action"); TR 73-74 (FDA addressing evidentiary use of CME sponsorship) (cited in WLF v. Henney, 202 F.3d at 336); TR 32, 60 (FDA discussing evidentiary use of reprint distribution); see also TR 41, 42, 43, 45, 58 (WLF arguing that FDA is permitted to bring misbranding actions under sections 301(a) and 301(d), [21 U.S.C. §§ 331(a) and (d)] , even under district court injunction); 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)(cited in WLF v. Henney, 202 F.3d at 336); Nature Food Centres, Inc. v. United States, 310 F.2d 67, 70 (1st Cir. 1963) (approving introduction of transcription of lectures as evidence of defendant's intended use); United States v. Millpax, Inc., 331 F.2d 152, 154 (7th Cir. 1963) (testimonials may be used to establish intended use of article as drug); 21 C.F.R. §§ 201.128 and 801.4.

That a manufacturer's expressions -- direct or through the apparent adoptions of the words of others -- may be used as evidence of its intent does not itself violate the First Amendment. Wisconsin v. Mitchell, 508 U.S. 476, 489 (1993) ("The First Amendment . . . does not prohibit the evidentiary use of speech to establish the elements of a crime or to prove motive or intent."); see also Dawson v. Delaware, 502 U.S. 159, 165 (1992) ("The Constitution does not erect a *per se* barrier to the admission of evidence concerning one's beliefs and associations . . . simply because those beliefs and associations are protected by the First Amendment). And although the Mitchell case involved an assault, the cases cited by the Court demonstrate that the holding that speech may be used as evidence of motive or intent is not limited to cases in which the prohibited act is one that is *malum in se*, as your petition suggests. For example, in Haupt v. United States, 330 U.S. 631 (1947), the defendant was convicted of treason on the basis of acts including helping his own son to get a job; providing the son food and shelter, and buying a car for the son's use, where those acts were found to be motivated by prohibited goals, as evidenced by the defendant's prior statements. Clearly, the underlying acts were not culpable absent the prohibited intent, evidenced by speech. Likewise, failing to grant someone partnership, the action in dispute in Price Waterhouse v. Hopkins, 490 U.S. 228, 251-252 (1989), is not inherently illegal, but was only prohibited where motivated by sexual discrimination, which the plurality believed could be established by the comments of voting partners. Accord Saxe v. State College Area Sch. Dist., 240 F.3d 200, 208 (3d Cir. 2001) ("we see no constitutional problem with using an employer's offensive speech as evidence of motive or intent in a case involving an allegedly discriminatory employment action").

In oral argument before the Court of Appeals, counsel for Washington Legal Foundation disputed FDA's interpretation that the FDCA as amended by FDAMA and the CME guidance do not independently prohibit speech. But WLF agreed that in an action for violations of section 301 of the statute, FDA could seek to establish the manufacturer's intended use of the product by introducing evidence of the manufacturer's dissemination of truthful, nonmisleading reprints of enduring materials addressing unapproved new uses of the manufacturer's products, as well as evidence of the manufacturer's sponsorship of CME at which such uses were discussed:

Mr. Rein: If the manufacturer's method of distributing the article, taken in context, whether it's by the proximity to the shipment, whether it's by the totality of the message amounts to a claim for a use that the manufacturer has not established in the statute to where remedy lies. That's not what this case is about. This case is not about Wisconsin v. Mitchell.

The Court: But that could be, even a peer reviewed piece could be used in that context. Right?

Mr. Rein: Right.

The Court: Even a pure article from the New England Journal of Medicine you concede in a misbrand [sic], in a suit, criminal case against the manufacturer arguing, claiming that they are marketing this for off-label purpose, that article from the New England Journal of Medicine could be used as evidence. You would argue that it isn't. Right? It wouldn't be a First Amendment problem.

Mr. Rein: *We're not claiming the First Amendment precludes it from being used as evidence --*

The Court: Right. Okay.

Mr. Rein: That is, it is, the fact that you send it out is conduct.

TR 50-51(emphasis added); see also TR 45 (WLF counsel indicating that where "the Government sought to bring a case . . . of improper shipment or a case of misbranding," these were permissible because they address "substantive violations and they address the conduct");⁷ TR 43, 51, 75 (WLF counsel agreeing that FDA may use distribution of reprints or support of CME as evidence of manufacturer intent in a misbranding action).

WLF's brief to the Court of Appeals was similarly consistent with the FDA position explained above:

There is no dispute here that a statement by a manufacturer generally may be introduced into evidence in a proper proceeding. That such a statement may possibly be used later as evidence in one context, however, detracts not a whit from its First Amendment protection. To illustrate, the statement "go buy a gun" may be a fully protected exhortation, or it may be a statement made in furtherance of a criminal conspiracy to commit murder. In the latter case, if a murder is committed or attempted, the statement may be introduced into evidence at trial. Similarly, a racial epithet may be a fully protected expression, but nonetheless may constitute evidence of a "hate crime." Wisconsin v. Mitchell, 508 U.S. 476, 490 (1993). Indeed, in one famous case, the Supreme

⁷ See also Pittsburgh Press Co. v. Pittsburgh Comm'n on Human Relations, 413 U.S. 376, 389 (1973) (First Amendment interest in commercial speech outweighed by government interest where restriction is incidental to valid limitation on economic activity, and thus commercial activity to which speech relates is itself illegal).

Court rejected a prior restraint against re-publication of a copy of the classified "Pentagon Papers," yet at the same time warned that the re-publication itself could lawfully be used as evidence should the publisher be prosecuted for violation of the national security laws. See New York Times Co. v. United States, 402 U.S. 713, 730 (1971) (Stewart, J., concurring).

Brief for Appellee Washington Legal Foundation, at 25.⁸

WLF consequently agreed that the statute and CME guidance present no facial First Amendment difficulties, in light of the government's statement that the statute and guidance create no *per se* bar or prohibition to dissemination of truthful, nonmisleading information about unapproved new uses of approved medical products and that this potential evidentiary use is the only consequence of these practices. See WLF v. Henney, 202 F.3d at 336 ("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") (citing TR 52, 66-68, 69); *id.* (noting agreement between WLF and FDA that neither Act nor CME facially violates First Amendment). It was on this basis that the Court of Appeals ruled that the case was moot and vacated in relevant part the decisions and injunction of the District Court. 202 F.3d at 336. FDA continues to stand behind the interpretation of the statute it expressed at oral argument, and the Federal Register notice and FDA's enforcement policy are consistent therewith and with the facial requirements of the First Amendment.

To elaborate, here is how distribution of reprints or sponsorship of CME, other than in a manner consistent with the specified safe harbors, may be used as evidence of manufacturer intent. When FDA brings an action alleging a violation of 21 U.S.C. §§ 331 or 355(a), the trier of fact will consider whether or not the manufacturer intended that its product be used for a use not approved by FDA. The manufacturer's intent will necessarily be determined on a case-by-case basis, looking at the totality of the facts and circumstances. Accord TR 41, 50, 51 (WLF arguing that distribution of reprints must be judged in context). The trier of fact will take into account the full body of evidence. If evidence of distribution or sponsorship activity forms part of the basis of FDA's claim, the trier of fact will consider the context of that activity and any other indicators of independence in assessing the manufacturer's objective intent.

FDA regulates products accounting for 22 cents out of every consumer dollar spent in the United States. Accordingly, when deciding whether to recommend court enforcement action,⁹ FDA considers the public health or other statutory interest to be served, the potential deterrent value of the litigation, and the likelihood of success, among other factors. Because FDA must choose carefully where to deploy its limited resources, FDA is unlikely to initiate an enforcement action where the only evidence of an unapproved intended use is the distribution of enduring materials or sponsorship of CME. You should know that the letter referenced in your citizen's petition is consistent with this approach. Although that letter addresses the distribution of reprints, it also refers to a pattern of other statements, on the manufacturer's web site, indicating an intent that the product in question be used for unapproved new purposes. Likewise, the letter referenced by the Coalition of Healthcare Communication also addresses multiple aspects of a promotional display

⁸ Filed in Washington Legal Foundation v. Henney, No. 99-5304, (D.C.Cir.) (November 8, 1999). A copy of this brief is on file with Dockets Management.

⁹ FDA does not have independent litigating authority. 21 U.S.C. § 337.

that indicate the manufacturer's intent that several of its products be used for unapproved uses -- including investigational products that had not been approved for any use. Thus, FDA's Federal Register Notice and its enforcement policy remain consistent with its position before the Court of Appeals and present no facial First Amendment problem.¹⁰

II. The District Court ruling with regard to the enduring material guidances does not bar the Federal Register notice and FDA's activities consistent with it.

As FDA's current policy, reflected in the Federal Register notice, is fully consistent with the positions of both FDA and WLF that led to the D.C. Circuit's vacatur of the district court's decision, that policy is also not barred by the district court's prior rulings.¹¹ FDA's current policies and actions do not violate any remaining portion of the district court's original injunction. Indeed, WLF litigated this exact issue before the same district court that issued the injunction, raising the argument that unappealed portions of the district court's decisions regarding the enduring material guidances conflicted with the Federal Register notice, and the court rejected WLF's argument. Washington Legal Foundation v. Henney, 128 F. Supp. 2d 11, 15 (D.D.C. 2000) (holding that "injunction has been wholly vacated by the Court of Appeals"); *id.* (holding that Court of Appeals "vacated all of this Court's previous constitutional rulings on the matter"). Moreover, at oral argument before the D.C. Circuit, WLF urged the court to leave the injunction standing on the grounds that it had never prevented FDA from instituting misbranding actions under sections 301(a) and 301(d) in the first place. See TR 43, 41, 42, 45, 58. Since this is exactly what FDA asserts authority to do in the Federal Register notice, by WLF's own terms, even if some relevant portion of the injunction were found to survive the Court of Appeals' decision -- an issue that WLF has already litigated and lost -- it would not preclude FDA's present policy and future enforcement action in compliance therewith.

Just as no injunction bars the Federal Register notice, collateral estoppel arising from the prior litigation does not preclude FDA from announcing the policy described in the Federal Register notice and acting consistently with it. While an individual litigant may raise a First Amendment objection to the use of his distribution of reprints or sponsorship of CME as evidence of his intent in a case brought against him for introduction of a violative product into interstate commerce, WLF v. Henney, 202 F.3d 331, 336 n.6 (D.C.Cir. 2000); accord 65 FR 14287 (March 16, 2000), FDA will not be precluded from pursuing that action and taking a contrary position on the use of that evidence. Most obviously, the parties to such an action will not be the same as those in the prior litigation, so no estoppel can lie. See United States v. Mendoza, 464 U.S. 154, 158 (1984) (offensive nonmutual collateral estoppel will not lie against United States).¹²

¹⁰ To the extent that either letter could be read to suggest that the FDCA contains an independent prohibition against the dissemination of truthful, nonmisleading reprints of articles or textbook excerpts regarding unapproved new uses of approved medical products, the letters suggested an erroneous reading of the statute.

¹¹ Although your petition speaks broadly of the preclusive effect of the district court's decisions, we understand your argument to be limited to the evidentiary use of reprint distribution, since the rulings with regard to the CME guidance were expressly vacated by the Court of Appeals. Washington Legal Foundation v. Henney, 202 F.3d at 337.

¹² Nor will such an action involve the same factual or even the same legal issues as were involved in WLF's prior facial challenge to the enduring material guidances. See Montana v. United States, 440 U.S. 147, 153 (1979) (collateral estoppel requires identity of legal or factual issue actually and necessarily decided by prior case).

Likewise, the view that, if WLF itself brings suit to challenge the Federal Register notice, collateral estoppel will allow it automatically to prevail is also flawed. First, your petition asserts that the District Court's rulings, finding the enduring material guidances and the policies reflected therein to be unconstitutional, subsume the conclusion that it would be unconstitutional for FDA to present the fact of reprint distribution as evidence of the manufacturer's intent in an action for introduction of a misbranded product into interstate commerce. However, you provide no citation to any of the District Court's opinions to support this reading. In fact, those opinions demonstrate that the District Court understood the enduring material guidances as a direct and independent restriction on speech, to be used by FDA when it could not stop the product itself from entering the market, and made its ruling on this basis. As the court explained,

For a brand-new drug, . . . the pharmaceutical company cannot manufacture or introduce the drug into interstate commerce without FDA approval. See 21 U.S.C. § 355(a). However, the drugs subject to off-label prescriptions are *already* in interstate commerce, so the obvious restriction on conduct is unavailable. Therefore, one of the few mechanisms available to FDA to compel manufacturer behavior is to constrain their marketing options; i.e., control the labeling, advertising and marketing. *If a manufacturer is proscribed from distributing enduring materials and/or sponsoring CME seminars that address that manufacturer's product absent FDA approval of that use, that proscription provides a strong incentive to get the use on-label, in light of the connection between marketing and sales.*

13 F. Supp. 2d at 72 (second emphasis added). In fact, in its later opinion, the district court itself invited FDA to file misbranding actions, noting that "to more stringently enforce its statutory authority to prosecute misbranding" would be, in that court's view, a more direct means of "effectuating the substantial government interest in encouraging manufacturers to seek FDA approval of off-label uses." WLF v. Henney, 56 F. Supp.2d 81, 87 (D.D.C. 1999). Such an enforcement action must be based on evidence that demonstrates the manufacturer's intent that his product be used for an unapproved new use, and that is all that FDA maintains today -- that it may use any and all evidence, circumstantial or direct, to support its case, including a manufacturer's distribution of reprints.

In fact, the district court's opinion adopted the view of the enduring material guidances taken by WLF itself in its summary judgment papers, where WLF repeatedly characterized the enduring material guidances as "prophylactic" measures and "bans." See, e.g., Memorandum in Support of Plaintiff's Motion for Summary Judgment,¹³ at 3, 11, 25; see also *id.* at 14-15 (citing examples of FDA refusing to grant advance clearance to manufacturers' plans to distribute reprints); *id.* at 35 (referring to guidances as regulations). These papers clearly indicated that WLF was arguing against an independent, prior ban and not about the possibility of the later evidentiary use of this manufacturer activity: WLF argued specifically that "FDA bears a heavy burden in justifying any such *proscriptive* ban on speech; *the constitutionally preferred remedy is vigorous after-the-fact*

¹³ Filed in Washington Legal Foundation v. Friedman, Civ. Act. No. 1:94CV01306(RCL) (D.D.C.) (November 24, 1997). [hereinafter "WLF Memorandum"]. A copy of this memorandum is on file with Dockets Management.

enforcement in the event of a specific violation." WLF Memorandum at 25 (emphases added). Cf. WLF v. Henney, 202 F.3d at 335 (noting that WLF understood both CME guidance and FDAMA provision and policies as "independently banning" speech).

Second, your petition argues that in not addressing on appeal the district court's ruling with respect to the enduring material guidances, FDA abandoned its appeal with respect to an implied ruling that FDA could not constitutionally bring a misbranding action against a manufacturer if it uses evidence that the manufacturer had distributed enduring materials as a means of establishing the manufacturer's intent.¹⁴ As explained above, FDA disputes that the district court's ruling on enduring materials included this conclusion at all. But if one assumes that the district court's ruling included this basis, FDA did not abandon its appeal on this issue. After all, FDA's position in appealing the ruling on the unconstitutionality of FDAMA clearly espoused the interpretation that this new statutory section, which superseded the enduring material guidances, accord WLF v. Henney, 56 F. Supp. 2d 81, 83 (D.D.C. 1999), provided a safe harbor of circumstances in which FDA could not make evidentiary use of the fact of reprint distribution in a misbranding action. For a safe harbor to exist, there must be something to harbor against, and so FDA's position clearly included the assertion that, for acts of distribution not conforming to the provisions of FDAMA, FDA may on a case-by-case basis use that distribution as evidence of the manufacturer's intent in a subsequent enforcement action. Indeed, the Court of Appeals understood this to be FDA's position, WLF v. Henney, 202 F.3d at 336, and it was with this understanding of the issues before it that the Court of Appeals ruled that there was no constitutional controversy between the parties. Thus, if this "evidentiary use" policy was embedded in the District Court's ruling on the enduring material guidances, it was equally embedded in the ruling on FDAMA. See WLF v. Henney, 56 F. Supp.2d 81, 84 (D.D.C. 1999) (holding that "the FDAMA largely perpetuates the policies held unconstitutional by the Court" in its opinion invalidating the enduring material and CME guidances and their underlying policies); *id.* at 85 n.5. Consequently, the conclusion that evidentiary use violates the First Amendment was raised to the Court of Appeals in appealing the district court's ruling on FDAMA and was vacated by that Court's ruling.¹⁵ Under these circumstances, no collateral estoppel can lie.

For the foregoing reasons, FDA declines to withdraw the Federal Register notice and to change its policy regarding the potential evidentiary use of reprint distribution or CME sponsorship in actions to enforce substantive violations of section 301 of the FDCA.

¹⁴ With the effective date of FDAMA and its implementing regulations, the specific enduring material guidances were superseded and thus no longer used by FDA. For that reason, any appeal with respect to the enduring materials guidances themselves would have been moot. See Memorandum of Points and Authorities in Opposition to Plaintiff's Motion for Summary Judgment and in Support of Defendants' Cross-Motion for Summary Judgment, filed in Washington Legal Foundation v. Friedman, Civ. Act. No. 1:94CV01306(RCL) (D.D.C.) (December 24, 1997), at 17 (stating that once FDAMA became effective, "the October 1996 Guidance Documents will be superseded by statute . . . , thereby mooting the issues WLF has raised herein with respect to those Guidance Documents") (copy on file with Dockets Management). As explained below, however, FDA's appeal continued to address all policies reflected in the guidance documents or the background of the issue that also remained under the superseding FDAMA provisions. Thus, the agency did not abandon the position that distribution of reprints or sponsorship of CME may both be used as evidence of manufacturer intent in a misbranding action.

¹⁵ Indeed, the Court of Appeals noted only that the enduring material guidances themselves were unenforceable as a result of their being superseded and because FDA had not challenged the district court decision and injunction so far as they pertained to those guidances themselves. WLF v. Henney, 202 F.3d at 334 n.4 (referring only to enduring material guidances, and not to broader policies).

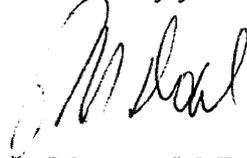
III. FDA's CME guidance reflects a safe harbor and FDA declines to alter it.

Your petition finally requests that FDA issue additional guidance regarding manufacturer sponsorship of CME. FDA's existing CME guidance identifies circumstances in which FDA has committed that it will not use the manufacturer's activities as evidence in an enforcement action. In essence, these are circumstances in which FDA believes that manufacturer support of CME would not demonstrate the manufacturer's intent that its product be used for an unapproved new use. The description of this safe harbor does not mean that FDA necessarily will bring an action in any case not clearly falling in the heartland of the CME guidance. The decision to bring any action will be made on a case-by-case basis, taking into account all of the facts and circumstances, as is the case in any exercise of prosecutorial discretion. Neither the presence nor absence of any of the factors discussed in the CME guidance is necessarily dispositive in FDA's determination of whether it has adequate evidence to support a charge of misbranding, although as the Federal Register notice states, FDA will consider these factors in its overall assessment of a manufacturer's activities. Given the case-specific nature of the determination whether or not to bring a misbranding action, and if so, what evidence to introduce, FDA has no current plan to expand or alter its CME guidance. Consequently, we deny your request.

IV. Conclusion

For the reasons expressed above, FDA declines your request to withdraw the March 16, 2000, Federal Register notice summarizing WLF v. Henney and to reinstate adherence to the full terms of the district court injunction vacated by the Court of Appeals. FDA also declines at this time to provide additional guidance regarding manufacturer sponsorship of CME. Because FDA is committed to respecting First Amendment rights as well as protecting the public health, it will continue to educate its enforcement personnel about the appropriate manner in which to consider manufacturer actions of distribution of reprints or sponsorship of CME regarding unapproved new uses of an approved product, and may use this activity as evidence of the manufacturer's intended use.

Sincerely yours,



Margaret M. Dotzel
Associate Commissioner for Policy

Docket no. 01P-0250

**Materials referenced in FDA response,
dated January 28, 2002,
to citizen petition of Washington Legal Foundation**

3399 02

AM29 P3:18

- Tab A:** Transcript of Oral Argument in Washington Legal Foundation v. Henney, No. 99-5304, argued January 10, 2000, before the United States Court of Appeals for the District of Columbia Circuit.
- Tab B:** Brief for Appellee Washington Legal Foundation, filed in Washington Legal Foundation v. Henney, No. 99-5304, (D.C. Cir.) (November 8, 1999).
- Tab C:** Memorandum in Support of Plaintiff's Motion for Summary Judgment, filed in Washington Legal Foundation v. Friedman, Civ. Act. No.1:94CV01306 (RCL) (D.D.C.) (November 24, 1997).
- Tab D:** Memorandum of Points and Authorities in Opposition to Plaintiff's Motion for Summary Judgment and in Support of Defendants' Cross-Motion for Summary judgment, filed in Washington Legal Foundation v. Friedman, Civ. Act. No.1:94CV01306 (RCL) (D.D.C.) (December 24, 1997).