

**UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF COLUMBIA**

**WASHINGTON LEGAL FOUNDATION,**

Plaintiff,

v.

**MICHAEL A. FRIEDMAN, M.D.,** in his  
official capacity as Acting Commissioner,  
Food and Drug Administration,

and

**DONNA SHALALA,** in her official  
capacity as Secretary, U.S. Dep't of  
Health and Human Services,

Defendants.

Civil Action No. 1:94CV01306  
(RCL)

**MEMORANDUM IN SUPPORT OF PLAINTIFF'S  
MOTION FOR SUMMARY JUDGMENT**

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## **I. INTRODUCTION AND SUMMARY**

This action by the Washington Legal Foundation ("WLF") challenges the constitutionality of sweeping restrictions on speech imposed by the United States Food and Drug Administration ("FDA"). It seeks to vindicate the First Amendment rights of pharmaceutical and medical device manufacturers to disseminate, and of physicians and other health care professionals to receive, medical and scientific information and data concerning lawfully marketed drugs and medical devices.

Congress has granted to FDA the limited authority to require pre-marketing approval of new drugs and certain medical devices and to base approval upon a showing of safety and efficacy for a particular use or uses. As FDA concedes, however, Congress has not given FDA any authority to regulate the practice of medicine. Drugs and devices that are approved by FDA for particular uses therefore may be, and frequently are, used by physicians in treatment regimens other than those set forth in the label approved by FDA.

FDA has admitted in discovery that such "off-label" uses are both widespread and beneficial, particularly in important fields such as oncology (where medical advancements routinely outpace the FDA approval process) and pediatrics (where the ability to conduct the controlled studies necessary for FDA approval is limited). In areas such as these, off-label uses serve not only as a necessary complement to labeled uses, but often constitute the standard of medical practice. As a result, there is a very substantial body of literature, including textbooks and scientific reports and analyses, that is not confined to approved (or "on-label") uses, but includes -- and in many instances focuses on -- off-label uses.

Because of the admitted benefits and prevalence of off-label uses in patient treatment, it is self-evident (and FDA has acknowledged, as it must) that treating physicians should have as much information as possible concerning such uses. Nevertheless, FDA has essentially prohibited pharmaceutical manufacturers from communicating with physicians and other health care professionals concerning off-label uses. FDA's restrictions, which apply only to communications by manufacturers (over whom FDA has regulatory authority), extend even to the dissemination by manufacturers of standard medical textbooks and reprints of articles previously published in peer-reviewed medical and scientific journals.

Thus, despite the unfettered discretion of physicians and patients concerning treatment regimens and the obvious benefit to doctors of having as much information as possible in reaching treatment decisions, FDA seeks to suppress information on off-label uses when coming from the manufacturers and their representatives who often are the most knowledgeable sources of such information and have the strongest incentive to make such information widely available. As a consequence, FDA has deprived and is depriving treating physicians of important scientific information -- indeed, in some instances, life-saving information -- concerning off-label uses.<sup>1</sup>

FDA's broad content- and speaker-based prohibitions silence a wide array of truthful scientific speech concerning matters of utmost importance to physicians and their patients. Such restrictions cannot withstand the rigorous scrutiny required by the Supreme Court in its First Amendment jurisprudence. FDA's apparent rationale for its restrictions -- the supposed

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<sup>1</sup> This challenge relates only to the dissemination by manufacturers to physicians and other health care professionals of scientific and medical information and data concerning prescription drugs and devices. It does not involve advertisements or other communications directed to consumers; nor does it concern non-prescription drugs or devices.

possibility that some manufacturer communications on off-label uses might be unsupported or untruthful and thereby lead to potentially unwise treatment decisions -- cannot justify a ban that deprives physicians of vast amounts of truthful information that otherwise would be available concerning legal off-label uses. Indeed, FDA's prophylactic ban is the antithesis of a narrowly tailored restriction, which the First Amendment requires if there is to be any limitation on speech.

FDA's ban also must be invalidated because any legitimate agency interests in regulating this scientific speech can be satisfied by far less onerous rules, some of which are already in place, that would not simultaneously stifle important scientific communication. For example, this action does not challenge certain of FDA's restrictions that may provide objective indicia of scientific quality or truthfulness, such as the requirement that reprinted articles be from legitimate peer-reviewed journals or the analogous provisions with respect to textbook distribution and continuing medical education ("CME") symposia. In addition, WLF does not here oppose any requirement that manufacturers disclose their interests, or the absence of FDA approval for a particular use, when communicating scientific information concerning off-label uses to doctors. In light of the overwhelming enforcement tools available to FDA and the punishments the marketplace would impose in the event that any false or misleading information were actually disseminated, such disclosures are more than adequate to protect any legitimate governmental interests.

Whether evaluated under the strict scrutiny applied to restrictions on fully protected scientific speech or under the somewhat less demanding (but still rigorous) standards applied to restrictions on commercial speech, FDA's policies cannot be reconciled with the First Amendment. Because there are no genuine factual issues concerning the nature of FDA's



activities and their impermissible suppression of truthful speech, WLF is entitled to summary judgment on its claims.

## II. UNDISPUTED FACTS

### A. FDA's Regulatory Regime And Its Limits

FDA regulates various aspects of the medical and pharmaceutical industries under, inter alia, the Federal Food, Drug, and Cosmetic Act of 1938, as amended, 21 U.S.C. § 301 et seq. ("the FDCA"), and the Medical Device Amendments of 1976, as amended, 21 U.S.C. §360c et seq.<sup>2</sup> One of FDA's functions is to approve new drugs sought to be introduced into interstate commerce as safe and effective for an intended use. 21 U.S.C. § 355(a).

In contrast to its role in approving drugs for sale, FDA does not regulate the practice of medicine. Accordingly, once a drug is approved, FDA does not control physicians' actual prescription practices for that drug. FDA acknowledges that "once a [drug] product has been approved for marketing, a physician may prescribe it for uses or in treatment regimes of patient populations that are not included in approved labeling." 59 Fed. Reg. 59820, 59821 (Nov. 18, 1994) ("Notice") (quoting FDA Drug Bulletin) (attached as Exhibit 3 hereto). Furthermore, "FDA has long recognized the legitimacy of physicians' use of drugs outside the approved labeling within the context of the practice of medicine." Temple Ex. 4 at 2703; accord, Hubbard

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<sup>2</sup> For the most part, the distinctions between prescription drugs and medical devices are not pertinent to the First Amendment issues addressed in this action. Accordingly, to avoid unnecessary repetition, we generally refer to drugs, rather than drugs and devices. However, except as specifically noted, the discussion is equally applicable to communications concerning medical devices.



Tr. 60, 124, 142, 147; Tart Tr. 148; Temple Tr. 31; Rose Tr. 43.<sup>3</sup> “FDA has no statutory charge or desire to interfere with [the] patient-physician relationship.” Hubbard Tr. 60-61.

**B. Prevalence And Importance Of Off-Label Uses**

The prevalence and importance of off-label uses in medical practice is beyond dispute. A recent study by the General Accounting Office determined that off-label uses range from “clearly experimental use to standard therapy and even to state-of-the-art treatment. . . . [F]or a specific form of cancer, a drug given off-label may have proven to be more beneficial than any drug labeled for that cancer.” U.S. General Accounting Office, Off-Label Drugs: Reimbursement Policies Constrain Physicians in Their Choice of Cancer Therapies, GAO/PEMD-91-14 at 11 (1991).<sup>4</sup>

FDA does not dispute the importance and benefits of off-label uses. “[P]ublic health may benefit from these off-label uses.” Tart Tr. 153; accord, Hubbard Tr. 60-61, 121 (agreeing that FDA “does not seek to prevent physicians from prescribing for unapproved indications” and that FDA “recognize[s] that the physician in clinical practice is well-equipped to make responsible, prescribing choices for both approved and unapproved uses”); Temple Tr. 13 (agreeing that

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<sup>3</sup> Excerpts of the following deposition transcripts appear in the appendix submitted herewith: William K. Hubbard, Associate Commissioner for Policy Coordination, who testified for FDA pursuant to Fed. R. Civ. P. 30 (b)(6); Janet L. Rose, Director of the Division of Drug Marketing, Advertising and Communications; Byron L. Tart, Director of Promotion and Advertising, Public Health Service Center for Devices and Radiological Health; and Robert Temple, Associate Director of the Center for Medical Policy and Director of the Office of Drug Evaluation.

<sup>4</sup> All emphasis is added throughout unless otherwise noted. A copy of the GAO Report appears in the Appendix.

“sometimes patient care responsibilities go beyond available data and physicians need to choose”), 66, 71, 78.

Moreover, FDA itself recognizes that off-label uses are so widespread in certain fields that such uses constitute the standard of good medical care. Hubbard Tr. 59 (concurring that “off-label use is often essential to good medical practice, and in some areas -- oncology and pediatrics among them -- off-label uses constitute a significant portion of standard therapy”); accord, id. 76; Tart Tr. 159; Temple Tr. 71. For example, FDA acknowledges that the agency’s labeling regime “is not particularly important to oncologists” because “they are getting their information not from the label” but “from colleagues in the practice and from journals and other scientific literature.” Hubbard Tr. 139; accord, Temple Ex. 4 (suggesting that “unlabeled indications [constitute] 60% of cancer treatment”); Temple Tr. 50 (“a lot” of off-label use in oncology). Indeed, “oncology is moving so fast, and physicians ... are using so many combinations of oncology drugs that the label can’t catch up with treatment practice.” Hubbard Tr. 65-66. FDA “understand[s] that and ha[s] no desire or intent to stop” oncologists from making off-label uses of products that a physician determines are appropriate. Hubbard Tr. 66-67. Oncologists agree that FDA labeling is of limited importance in that practice. Fox Dec. ¶ 3 (“[T]he medical community’s knowledge regarding the safety and efficacy of FDA-approved products inevitably outpaces FDA-approved labeling. Physicians who regularly work with FDA-approved drugs and medical devices learn of safe and efficacious uses for those products that are not included within the labeling.”)<sup>5</sup>

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<sup>5</sup> The Declaration of Dr. Henry B. Fox, an oncologist and physician-member of WLF, is submitted herewith.

Similarly, off-label uses occur so frequently in pediatrics that many are tacitly recognized as the norm. Temple Tr. 54. One reason is that the studies necessary to gain approval for use in children are sometimes prohibitively expensive, even where the drug in question already is approved for treating adults. See Speech of FDA Commissioner David Kessler to the American Academy of Pediatrics, Oct. 14, 1992 ("Kessler Speech")<sup>6</sup>; accord, Hubbard Tr. 164 (difficulties presented by small pool of patients). FDA also acknowledges that "sensitive political or public relations" concerns may inhibit manufacturers from employing children as the subject of clinical trials. Hubbard Tr. 77-78. As a result, "[t]he labeling of drugs and biologics for use in children lags well behind the clinical patterns of use. For many approved drugs, the labeling carries little or no information about use in children." Kessler Speech, supra.

FDA has acknowledged that off-label uses also are "pervasive" in the device context and that "[t]he medical community believes that such use is in the best interest of the patient." Tart Ex. 1 at 3003; Tart Tr. 28. For example, FDA admits that there are some 30,000-70,000 off-label uses annually of the device known as a "pedicle screw." Tart Tr. 139; App. Ex. 9. FDA also is aware that the off-label use of devices such as urologic lasers is so commonplace as to constitute the standard of care for certain conditions. Tart Tr. 159.

As suggested by the foregoing examples, the fact that a use is off-label rather than on-label has no necessary correlation to the benefits of that use. "[T]he fact that [a use] is not an approved indication should not be viewed . . . as some sort of determination by FDA that the use is inappropriate." Hubbard Tr. 141; accord, Temple Ex. 2 at 689 ("[t]he absence of an indication on the labeling does not mean that the drug is not useful for that purpose"). To the contrary,

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<sup>6</sup> A copy of the text of the Kessler speech is submitted herewith.

FDA recognizes that various factors may preclude beneficial uses from being on-label. See Hubbard Tr. 65-66, 79-80, 134-35, 164; Temple Tr. 33, 56-57, 60.

Most significantly, as set forth above with respect to oncology, the speed of medical advances often outstrips FDA's ability to keep pace. Because "it takes the time to get an application together for an approved use and then have FDA review it, . . . [y]ou always are going to have off-label use occurring before the labeling gets on the drug." Hubbard Tr. 135. In addition to the delay resulting from the required clinical trials, the agency's limited resources retard the speed of the approval process after a supplemental application for a new use is filed. Hubbard Tr. 79-80.<sup>7</sup>

Economic considerations also may play a role in determining whether beneficial uses of drugs are submitted for approval. FDA recognizes that, in cases where an off-label use benefits only a relatively small number of patients, manufacturers may be reluctant to expend the sums necessary to conduct well-controlled clinical trials if ultimate regulatory approval will not increase sales sufficiently to cover the costs incurred. Hubbard Tr. 164. FDA also recognizes that, in cases where a product is no longer protected by patent and therefore is subject to immediate copying by generic manufacturers, pioneer pharmaceutical manufacturers may have little incentive to expend the sums required to submit a supplemental application for a new use. Temple Tr. 60, 90.

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<sup>7</sup> A Note recently published in the Virginia Law Review addressing the same constitutional matters at issue in this action noted that "[t]he mean [FDA] review time during the period from 1989-1994 for new uses of currently approved drugs was 28.3 months." 83 Va. L. Rev. 991, 1005 (1997).

In sum, FDA “recognizes and accepts th[e] reality” that off-label uses are “often essential to good medical practice” and in some areas “constitute a significant portion of standard therapy.” Hubbard Tr. 59. “All of our physicians and scientists in the agency strongly believe in the concept of physicians being able to prescribe for off-label uses based on their own experience, knowledge, consultation with colleagues and other sources of information.” Hubbard Tr. 72.

**C. Importance Of Physicians’ Knowledge Concerning Off-Label Uses**

Because it recognizes the prevalence and importance of off-label uses in patient treatment, FDA also recognizes that “public health would be substantially impaired in this country if physicians were unable to make wise and informed use of drugs for unlabeled indications.” Hubbard Tr. 60. Such “informed use” requires that physicians have “reliable, up-to-date information regarding off-label uses on which to base their practice decisions.” Hubbard Tr. 60; see also Rose Tr. 128-29. Accordingly, FDA deems it “very appropriate” for doctors to obtain information about off-label uses. Hubbard Tr. 46; accord, id. 67, 72; Tart Tr. 155 (“the doctor should have as much information as he feels necessary to use that device or drug on his patient, and that physician is obligated to get that information”).

Reliable information is particularly important (and potentially scarce or inaccessible) in the realm of off-label uses, because one usual source of information -- the label -- is unavailable. Fox Dec. ¶ 10 (because so many cancer treatments are off-label, “I simply cannot place principal reliance on FDA-approved labeling in prescribing drugs to my patients. . . . Unless I can gain access to other sources of information regarding the latest medical information, I am unable to treat my patients properly.”); accord, Hubbard Tr. 72 (agreeing that physicians should “prescribe

for off-label uses based on their own experience, knowledge, consultation with colleagues and other sources of information”).

**D. FDA Restrictions On Speech Concerning Off-Label Uses**

Despite the prevalence and benefits of off-label uses and the acknowledged need for physicians to have the fullest possible information concerning such uses, FDA has intentionally and affirmatively sought to impede the dissemination of scientific information concerning off-label uses by one particularly knowledgeable group -- pharmaceutical and device manufacturers. See Hubbard Tr. 46, 63-64; Temple Tr. 14-15; Tart Tr. 19-20, 90, 123-24. Specifically, FDA has imposed substantial restrictions on manufacturer dissemination of articles reprinted from professional journals, see Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data, 61 Fed. Reg. 52800 (Oct. 8, 1996) (the “Reprint Guidance”), manufacturer dissemination of “medical textbooks and compendia,” see Guidance for Industry Funded Dissemination of Reference Texts, 61 Fed. Reg. 52800 (Oct. 8, 1996) (the “Textbook Guidance”), and manufacturer financial support for professional symposia and continuing medical education or “CME” seminars, see Draft Policy Statement on Industry Supported Scientific and Educational Activities, 57 Fed. Reg. 56412 (Nov. 27, 1992) (the “Draft Symposium Order”).<sup>8</sup> These are Exhibits 1 and 2 hereto, respectively.<sup>9</sup>

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<sup>8</sup> The “Draft” Symposium Order is operative and reflects FDA enforcement policy. See Hubbard Tr. 39-40, 44-45.

<sup>9</sup> The Reprint Guidance and Textbook Guidance were published together under one Notice in the Federal Register, which is Exhibit 1. These Guidances were issued subsequent to the Court’s decision denying FDA’s Motion to Dismiss this action. See Washington Legal Foundation v. Kessler, 880 F. Supp. 26 (1995). However, except for some changes with respect  
(continued...)

The distribution of textbooks and article reprints, which are known collectively as “enduring materials,” is restricted whenever a drug or device manufacturer is involved in the process in any manner. The Reprint Guidance bars manufacturers from disseminating articles reprinted from peer-reviewed professional journals unless, among other restrictions, the “principal subject” of the reprinted article is an FDA-approved (i.e., on-label) use and the article specifically reports the original study submitted to FDA for purposes of approving the labeled use. Reprint Guidance at 52801. Thus, if practice results or further research reveal beneficial off-label uses, any distribution of a reprint focusing on such uses is banned. Id.

The Textbook Guidance has similarly pervasive restrictions with respect to “reference texts, i.e., medical textbooks and compendia.” Id. at 52801. It bars manufacturers from disseminating books and compendia that focus primarily on any particular product(s) of the disseminating manufacturer or that have “a significant focus” on off-label uses of a manufacturer’s product. Id. Moreover, although the Guidance does not say so explicitly, it appears to contemplate only dissemination of entire textbooks (rather than particular chapters or sections pertinent to specific practice specialties); this would be consistent with FDA’s enforcement posture. However, distribution of entire books may be financially prohibitive or fundamentally impractical because much of the material would have no pertinence to physicians with distinct practice specialties. Even if the textbook satisfies all of the restrictions set forth in the Guidance, a manufacturer’s representative still is prohibited from “refer[ring] to, or otherwise

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(...continued)

to dissemination of textbooks, the enforcement policies reflected therein are substantially similar to policies in effect since at least 1991. This discussion focuses on the current policies as set forth in the 1995 Guidances and the 1992 Draft Symposium Order.

promot[ing], in any manner or at any time,” information printed in a reference text that “is not consistent with the [FDA] approved labeling for a product.” Id. at 52801.

FDA also places strict constraints on pharmaceutical and device manufacturers’ participation in scientific and educational activities (i.e., CME symposia) if off-label uses are discussed. Under the Draft Symposium Order, manufacturers may not support CME seminars and similar scientific programs that involve discussions related to the company’s product(s) unless the event is created and operated by an independent “program provider” pursuant to a detailed written agreement. See Draft Symposium Order at 56413-14. The written agreement must provide, inter alia, that the program provider controls the program content, including the selection of speakers, and the manufacturer cannot influence program content. Id.

Manufacturers that comply with all of the restrictions set forth in the Draft Symposium Order still cannot be assured that they have insulated themselves from administrative sanctions. Rose Tr. 32. FDA may also act on the basis of other factors indicating “improper” manufacturer influence on an event. Draft Symposium Order at 56414. These factors include, inter alia, (1) relationships between the manufacturer and program provider that might allow the manufacturer to influence program content; (2) “significant contacts” between “industry representatives” and speakers; (3) a focus on a single product of the manufacturer or a competing product; and (4) after the initial program presentation, any “further” dissemination by the manufacturer of information about company products discussed during the program. Id. FDA has indicated that it will rely “to the extent possible” on major accrediting organizations to ensure that symposia are “independent and nonpromotional.” Id.

FDA issued its guidances and orders despite the fact that it had little data concerning the extent of off-label uses of prescription drugs or devices or the harms that might have been



attributable to those uses. See Hubbard Tr. 74-76, 81-82; Temple Tr. 47-49; Rose Tr. 113, 119-20. Moreover, FDA officials admit that they have received few complaints about the promotion of off-label uses by manufacturers. Tart Tr. 76-77, 85-86, 113; Rose Tr. 121-22, 125-26.

Any presumption by FDA that manufacturers' speech concerning off-label uses must be misleading is undermined by FDA's allowance of such speech when it occurs in response to physician inquiries. FDA acknowledges that it permits manufacturers to respond to inquiries from physicians concerning off-label uses, as long as these inquiries are unsolicited, and that there is no material difference between such responses and the information that might be affirmatively provided by manufacturers in the absence of any inquiry. Tart Tr. 53-54 (admitting no difference in the information being provided). FDA's representatives could not explain the rationale for this starkly differing treatment of the same substantive information. Hubbard Tr. 177 (if the concern is that FDA cannot verify the "truth" when a manufacturer discusses an unapproved use, deponent unable to explain why FDA allows exception for manufacturer responses to unsolicited queries); Tart Tr. 101-02 (admitting rationale behind distinction not clear), 111-12 (deponent unable to explain why only those physicians who know enough to ask questions should get the information).

**E. Impact Of FDA's Restrictions And Enforcement**

FDA began in the early 1990s to vigorously enforce restrictions on manufacturer support for redistribution of articles and textbooks and manufacturer sponsorship of academic symposia and educational seminars. Tart Tr. 72-74. As discussed below, manufacturers as a consequence have substantially reduced their distribution of textbooks, article reprints, and similar written materials to physicians. See Rose Ex. 2 at 7211 (1994 memorandum noting "perception within

the pharmaceutical and publishing industries that [FDA] was impeding the distribution of . . . materials and the free flow of information"). FDA acknowledges that, because of this enforcement activity, some important information "is not likely to reach physicians as fast as it should." Temple Tr. 72. Several examples illustrate the positions taken by FDA.

In February 1992, Mead Johnson sought FDA preclearance to distribute a standard reference book, Hematology/Oncology Clinics of North America: Nutrition and Cancer ("NAC"). FDA refused to approve Mead Johnson's plan for distributing NAC through its sales representatives. Samp Aff. Ex. H.<sup>10</sup> Rather, FDA indicated that it would permit distribution only if physicians requested the book by means of a pre-printed business reply card with the text limited solely to a request for NAC, and only if the book delivery were made through an "appropriate mail delivery service" rather than by Mead Johnson representatives. Id.

The next month, Bristol-Myers Squibb Co. ("BMS") similarly sought FDA preclearance to distribute certain chapters (including publisher-abridged chapters) from a standard oncology textbook, DeVita, Hellman, and Rosenberg (eds.), Cancer. Principles & Practice of Oncology (J.B. Lippincott Co., 3d ed., 1989), to medical specialists. Samp Aff. Ex. B. The publisher, J.B. Lippincott Co. ("Lippincott"), was solely responsible for selecting the chapters to be distributed, which concerned the specialty areas of the intended recipients -- including lung cancer, surgery, radiation therapy, chemotherapy, and pulmonary complications of cancer. Nevertheless, FDA refused to approve the plans for distributing the excerpted chapters because the selections "contain[ ] chapters which discuss unapproved indications of Bristol-Myers Squibb oncology

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<sup>10</sup> The Affidavit of Richard A. Samp, Washington Legal Foundation, is submitted herewith.

products.” Samp Aff. Ex. B. FDA suggested that it would approve plans to distribute the textbook in its entirety, id., but the entire volume is too bulky and expensive to be a practical item for distribution. Also, doctors specializing in one aspect of oncology would have little interest in receiving portions of the text addressing unrelated aspects.

In April 1992, BMS sought FDA preclearance of its plan to distribute another standard medical reference book, Skeel (ed.), Handbook of Cancer Chemotherapy (Little, Brown & Co., 3d ed., 1991) (“Handbook”). See Samp Aff. Ex. I. Distribution was to be made by BMS sales representatives to oncologists, hematologists, pulmonologists, thoracic surgeons, and other non-oncologist physicians to acquaint them with chemotherapy and the various pulmonary complications of cancer. FDA refused to approve the distribution plan, stating such distribution “is violative due to discussions of unapproved uses.” Id. FDA indicated that the Handbook could be distributed by “an independent third party,” provided that BMS did not identify specific physicians to whom the Handbook was to be distributed. Id.

FDA’s policy of suppression extends to article reprints as well. For example, in 1991, FDA began requiring manufacturers to seek preclearance from FDA before distributing “Updates” published by Lippincott. See September 30, 1991 issue of FDC Reports, attached at App. Ex. 8. FDA refused to grant approval to the proposal of pharmaceutical manufacturer Bristol-Myers to distribute or finance distribution of certain Lippincott Update publications because the materials discussed off-label uses of Bristol-Myers products. In response, Lippincott informed FDA that the agency’s preclearance requirement would effectively close down the Update publication program, because Lippincott could not meet its monthly publication schedule if the publisher were obligated to submit copy to FDA for pre-publication review. Samp Aff. Ex.

A. Lippincott also protested that being required to submit its copy to any outside entity infringed on the publisher's editorial independence. Id.

As the exhibits reflect, FDA had no evidence that any of the information set forth in the enduring materials discussed above was false or misleading. Both the authors and the publishers of the materials were independent of the manufacturer that sought to distribute the materials further. Nevertheless, FDA's enforcement activities curtailed the speech of the publishers and the manufacturers -- and physicians' ability to receive beneficial speech -- by preventing distribution of truthful information about the manufacturers' products.

The effect of FDA's enforcement activities has not been limited to curtailing distribution of written materials. Drug and device manufacturers also have substantially reduced their support of CME seminars and similar symposia as a result of FDA's policies. This reduction in financial support has reduced -- and, in some cases, eliminated -- speech concerning off-label uses of drugs and devices. Tart Tr. 129-30. At least one FDA official recognized in October 1991 that the enforcement activities initiated earlier that year "are already having a chilling effect on the legitimate exchange and dissemination of state-of-the-art scientific information, with certain key companies suspending their investments in legitimate, non-promotional CME activities." Hubbard Ex. 10 at 7702.

In 1993, FDA sent warning letters threatening enforcement action to several manufacturers of spinal implants in connection with their dissemination at CME programs or symposia of information concerning the off-label use of bone screws in the pedicles of the spine. Tart Ex. 1 at 3005-06; App. Exs. 7, 9. In general, the 1993 letters stated that the manufacturers were in violation of the FDC Act for (1) supplying samples of their products for use during training sessions at the CME programs; (2) providing information regarding their products; and

(3) allowing doctors affiliated with the manufacturers to participate in demonstrating pedicle fixation. Id. The 1993 warning letters gave each manufacturer 15 days to correct its violation. Id. Failure to do so would have risked closure of the manufacturer's business and seizure of its entire stock of medical devices.

Before the 1993 warning letters were issued, leading professional organizations -- including the American Academy of Orthopedic Surgeons, the North American Spine Society ("NASS"), and the Scoliosis Research Society ("SRS"), and many teaching hospitals -- organized CME programs designed to familiarize doctors with pedicle fixation techniques. As a result of the 1993 warning letters, however, such training programs are no longer offered in the United States, and scheduled programs were canceled. Tart Tr. 129-31; App. Ex. 9; Bashook Aff. ¶ 3.

As with reprints and textbooks, FDA had no evidence that the communications it was suppressing at CME and similar symposia were false or misleading. See Tart Tr. 133. The speakers and the event organizers were independent of the manufacturer that planned to support the event financially. Nevertheless, FDA's enforcement activities restrained the speech of the program presenters and the manufacturers by barring distribution of truthful information about the manufacturer's products, and precluded physicians from receiving the information.

#### **F. FDA Reform Legislation**

The Food and Drug Administration Modernization Act (the "Modernization Act"), signed into law on November 21, 1997, addresses some of the most extreme aspects of FDA's policies and practices on communications concerning off-label uses. S. 830, 105th Cong., 1<sup>st</sup> Sess. (1997) (relevant provisions to be codified at 21 U.S.C. § 551 et seq.). The statute rejects the

contention that communications concerning off-label uses should be categorically prohibited as improper promotions. To some extent, the new statute should ameliorate certain of FDA's current policies with respect to the matters addressed.

While it reflects a step forward from some aspects of the restrictive FDA regime, however, the new legislation does not and will not resolve the constitutional issues raised by this action. The legislation does not address CME seminars and symposia at all; thus, FDA's current policies and practices on these matters under the Draft Symposium Order will remain in effect. Moreover, the legislation in all likelihood will not become effective for a full year. Modernization Act § 401 (to be codified at 21 U.S.C. § 557) ("amendments made by this section shall take effect 1 year after the date of enactment of this Act, or upon the Secretary [of Health and Human Service]'s issuance of final regulations"). In the interim, there is nothing to prevent FDA from enforcing its current restrictive policies.

Even as to the matters addressed, and without considering additional impediments to speech rights that may be imposed by FDA in its implementation of the legislation, serious First Amendment problems remain. In a bow to FDA's posture in the legislative process, even the reform statute places numerous -- and onerous -- conditions and burdens on the exercise of First Amendment rights. For example, a manufacturer may circulate articles and textbooks (unabridged) as a matter of right only if it has submitted to FDA a supplemental application for approval of a new use or certifies that it will do so within a specified period. See § Modernization Act 401 (to be codified at 21 U.S.C. § 551). In other instances, distribution is contingent on approval by the Secretary of an exemption application. In any event, materials may not be disseminated without submissions to FDA sixty days in advance (along with various other materials) and the Secretary may require the manufacturer also to distribute simultaneously

additional materials the Secretary orders. There are numerous other respects in which speech rights are circumscribed and encumbered. Thus, the statute on its face will not resolve the constitutional issues presented here for determination.

### III. **ARGUMENT**

#### A. **Summary Judgment Is Appropriate Where There Are No Genuine Issues Of Material Fact And The Moving Party Is Entitled To Judgment As A Matter Of Law.**

A court should grant summary judgment if the record reveals that there is "no genuine issue as to any material fact, and that the moving party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(c). Under Rule 56, "[o]nly disputes over facts that might affect the outcome of the suit under the governing law will properly preclude the entry of summary judgment. Factual disputes that are irrelevant or unnecessary will not be counted." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986).

When the nonmovant bears the burden of proof on an issue at trial, "the moving party need only demonstrate the absence of evidence supporting the non-movant's claim." Winn v. United Press Int'l, 938 F. Supp. 39, 41 (D.D.C. 1996), aff'd, 1997 WL 404959 (D.C. Cir. July 14, 1997). To avoid summary judgment, the nonmovant must do more than raise "some metaphysical doubt as to the material facts." Matsushita Electric Industrial Co. v. Zenith Radio Corp., 475 U.S. 574, 586 (1986). Rather, the nonmovant must demonstrate specific facts illustrating a genuine issue for trial. Celotex Corp. v. Catrett, 477 U.S. 317, 323 (1986). Where a rational trier of fact could not find for the nonmoving party based on the record taken as a whole, the motion for summary judgment should be granted. Matsushita, 475 U.S. at 586.



**B. FDA Bears The Burden Of Defending Its Restrictions On Speech.**

The First Amendment provides that Congress (and the states through the Fourteenth Amendment) “shall make no law . . . abridging the freedom of speech . . .” The freedom of speech is considered a “basic and fundamental” right, Cox v. Louisiana, 379 U.S. 559, 574, (1965), and is the “matrix, the indispensable condition, of nearly every other form of freedom.” Palko v. Connecticut, 302 U.S. 319, 327 (1937), overruled on other grounds, 395 U.S. 784 (1969). “The constitutional right of free expression is . . . intended to remove governmental restraints from the arena of public discussion . . . in the belief that no other approach would comport with the premise of individual dignity and choice upon which our political system rests.” Simon & Schuster, Inc. v. Members of the New York State Crime Victims Board, 502 U.S. 105, 116 (1991).

The First Amendment protects receivers of speech as well as speakers. “[I]t is now well established that the Constitution protects the right to receive information and ideas.” Kleindienst v. Mandel, 408 U.S. 753, 762 (1972) (quoting Stanley v. Georgia, 394 U.S. 557, 564 (1969)). See also Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc., 425 U.S. 748, 757 (1976) (freedom of speech “necessarily” protects the right to receive information); Martin v. City of Struthers, Ohio, 319 U.S. 141, 143 (1943) (same). Indeed, “[t]his right to receive information and ideas is fundamental to our free society.” Stanley, 394 U.S. at 564.

Because of the overriding importance of the right of free speech, the burden always is on the government to defend the restrictions it seeks to impose. See, e.g., Simon & Schuster, 502 U.S. at 118 (“the State must show that its regulation is necessary to serve a compelling state interest and is narrowly drawn to achieve that end”) (quoting Arkansas Writers’ Project, Inc. v.



Ragland, 481 U.S. 221, 231 (1987)); Boos v. Barry, 485 U.S. 312, 321 (1988) (“we have required the State to show that the regulation is necessary to serve a compelling state interest and that it is narrowly drawn to achieve that end”) (internal quotation marks omitted).

The government’s burden is particularly heavy in this case, because content- and speaker-based restraints on speech such as the ones at issue here are abhorrent to the interests protected by the First Amendment and therefore are subject to the strictest possible scrutiny. See Sable Communications of California v. Federal Communications Comm’n, 492 U.S. 115, 126 (1989) (content-based regulation subject to strict scrutiny); Turner Broadcasting System, Inc. v. Federal Communications Comm’n, 512 U.S. 622, 658 (1994) (“laws favoring some speakers over others demand strict scrutiny when the legislature’s speaker preference reflects a content preference”). Such speech restrictions are presumptively unconstitutional. Rosenberger v. Rector and Visitors of the University of Virginia, 115 S. Ct. 2510, 2516 (1995) (“[d]iscrimination against speech because of its message is presumed to be unconstitutional”); R.A.V. v. City of St. Paul, Minnesota, 505 U.S. 377, 382 (1992) (“[c]ontent-based regulations are presumptively invalid”); Simon & Schuster, 502 U.S. at 115 (“statute is presumptively inconsistent with the First Amendment if it imposes a financial burden on speakers because of the content of their speech”).

Even under the somewhat lesser protections applicable to commercial speech (which are inappropriate for the scientific and medical information at issue here, for the reasons discussed below), the First Amendment still imposes a significant burden on the government to justify any restrictions. City of Cincinnati v. Discovery Network, Inc., 507 U.S. 410, 416 (1993); Bolger v. Youngs Drug Products Corp., 463 U.S. 60, 68-69 (1983); Central Hudson Gas & Elec. Corp. v. Public Service Comm’n, 447 U.S. 557, 564-66 (1980); Kansas v. United States, 16 F.3d 436, 442 (D.C. Cir. 1994). As with fully protected speech, “[t]his burden is not satisfied by mere

speculation or conjecture; rather, a governmental body seeking to sustain a restriction on commercial speech must demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree.” Edenfield v. Fane, 507 U.S. 761, 770-71 (1993); see also Rubin v. Coors Brewing Co., 514 U.S. 476, 486 (1995); 44 Liquormart, Inc. v. Rhode Island, 116 S. Ct. 1495, 1509 (1996) (plurality opinion).

As demonstrated below, FDA cannot meet its burden, either under the strict scrutiny applied to restrictions on fully protected speech or under the commercial speech doctrine.

**C. FDA’s Guidelines And Policies Impermissibly Restrict Fully Protected Scientific Speech.**

**1. Scientific And Medical Information And Data Are Fully Protected Speech.**

Speech with scientific or academic value is at the core of the communications protected by the First Amendment. See, e.g., Keyishian v. Board of Regents, 385 U.S. 476, 484 (1957) (academic freedom is “a special concern of the First Amendment”); Miller v. California, 413 U.S. 15, 34 (1973) (First Amendment protection extends to works with “scientific value”). “[T]he First Amendment protects scientific expression and debate just as it protects political and artistic expression.” Board of Trustees of Leland Stanford Junior University v. Sullivan, 773 F. Supp. 472, 474 (D.D.C. 1991).

This otherwise fully protected speech does not become “only” commercial speech by virtue of the fact that a manufacturer paying to disseminate the speech has an economic interest in the product under discussion. To the contrary, the fact that the manufacturer “has an economic motivation” to support distribution of the information “would clearly be insufficient by itself to turn the materials into commercial speech.” Bolger, 463 U.S. at 67; cf. New York Times Co. v.

Sullivan, 376 U.S. 254, 266 (1964) (“[t]o avoid placing . . . a handicap upon the freedoms of expression, we hold that if the . . . statements would otherwise be constitutionally protected . . . , they do not forfeit that protection because they were published in the form of a paid advertisement”) (assessing protected status of allegedly libelous statement).

Moreover, aside from the case law that affirmatively establishes that scientific speech is fully protected, the speech at issue here exhibits none of the characteristics that would make it commercial speech. The Supreme Court has “characteriz[ed] the proposal of a commercial transaction as ‘the test for identifying commercial speech.’” Discovery Network, 507 U.S. at 423 (emphasis in the original) (quoting Board of Trustees of the State University of New York v. Fox, 492 U.S. 469, 473-474 (1989)). The activities at issue here -- e.g., mailing a textbook or an article reprint, presenting data at a symposium, etc. -- do not propose a commercial transaction. Thus, under the governing standard, the speech here is not commercial speech.

In addition, the speech here does not reflect any of the related characteristics that the Supreme Court has also used in identifying commercial speech.<sup>11</sup> For example, none of the parameters for classifying speech as commercial set out in Bolger is applicable here. See 463 U.S. at 66-67. The textbooks, article reprints, and symposia support are not “advertisements” in the common understanding of the term; even if they were, that would be insufficient to “compel the conclusion that they are commercial speech.” Id. at 66. Nor does the reference to a specific

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<sup>11</sup> The Court has been careful to maintain a definition that does not sweep too broadly in order “to ensure that speech deserving of greater constitutional protection is not inadvertently suppressed.” Discovery Network, 507 U.S. at 423 (quoting Bolger, 463 U.S. at 66). See also Central Hudson, 447 U.S. at 579 (Stevens, J., concurring) (“it is important that the commercial speech concept not be defined too broadly lest speech deserving of greater constitutional protection be inadvertently suppressed”).

product in textbooks, article reprints, or symposia presentations “by itself render [the communication] commercial speech.” Id.; see also Securities & Exchange Comm’n v. Wall Street Publishing Institute, Inc., 851 F.2d 365, 372 (D.C. Cir. 1988). Thus, the speech at issue here is not commercial.

Even if the speech here could be deemed a hybrid, including commercial and noncommercial aspects, whatever elements of the latter may exist are inextricably intertwined with the fully protected non-commercial elements, which therefore requires application of the strictest standard of First Amendment scrutiny. Riley v. National Federation of the Blind, 487 U.S. 781, 796 (1988); Board of Trustees of the State University of New York v. Fox, 492 U.S. 469, 474-75 (1989).<sup>12</sup> “[W]here, as here, the component parts of a single speech are inextricably intertwined,” courts “cannot parcel out the speech, applying one test to one phrase and another test to another phrase. Such an endeavor would be both artificial and impractical.” Riley, 487 U.S. at 796 (applying highest level of First Amendment review to arguably commercial elements of charitable solicitation).

**2. The FDA Guidelines And Policies At Issue Require Heightened Scrutiny Because They Are Content And Speaker Based.**

Rather than being subject to any lesser scrutiny, FDA’s actions and regulatory scheme in fact require heightened scrutiny, because they incorporate so many elements disfavored under First Amendment precedent. As discussed above, the two Guidances and the Draft Symposium

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<sup>12</sup> The FDA regulations here do not merely restrict sales pitches that happen to include protected speech, such as the home products demonstrations at issue in Fox. Rather, FDA’s restrictions here have demonstrably “prevent[ed] the speaker from conveying, or the audience from hearing, the[ ] noncommercial messages.” Fox, 492 U.S. at 475.

Order essentially foreclose manufacturer speech concerning off-label uses of their products. FDA bears a heavy burden in justifying any such proscriptive ban on speech; the constitutionally preferred remedy is vigorous, after-the-fact enforcement in the event of a specific violation. See, e.g., Boos, 485 U.S. at 312. It is also long-standing First Amendment doctrine that blanket speech bans are disfavored unless the government demonstrates that no other means can serve its legitimate goals. “Broad prophylactic rules in the area of free expression are suspect. . . . Precision of regulation must be the touchstone.” NAACP v. Button, 371 U.S. 415, 438 (1963).

Moreover, FDA’s policies rest on not just one but two suspect distinctions: they restrict both “the subjects about which persons may speak and the speakers who may address a public issue.” First National Bank of Boston v. Bellotti, 435 U.S. 765, 785 (1978) (acknowledging corporation’s free speech rights). FDA’s restrictions, which are triggered, inter alia, by a “significant focus” on off-label uses (Textbook Guidance at 52801), are properly categorized as content-based rules “by any commonsense understanding of the term.” Discovery Network, 507 U.S. at 426-429. Accordingly, the highest degree of First Amendment scrutiny applies. Sable Communications, 492 U.S. at 126.

FDA’s restrictions also are subject to strict scrutiny as speaker-based rules. According to the Supreme Court, speaker-based restrictions are constitutionally suspect when the restrictions are “concerned with the communicative impact of the regulated speech.” Turner Broadcasting, 512 U.S. at 658. FDA has made clear that the purpose of the restrictions at issue here is to prevent manufacturers -- but not other speakers -- from communicating to physicians and other health care professionals information regarding off-label uses of the manufacturers’ products. Such “differential treatment . . . suggests that the goal of the regulation is not unrelated to suppression of expression, and such a goal is presumptively unconstitutional.” Minneapolis Star

& Tribune Co. v. Minnesota Commissioner of Revenue, 460 U.S. 575, 585 (1983). Thus, because the regulations clearly “reflect the Government’s . . . aversion to what the disfavored speakers have to say,” strict scrutiny must be applied. Turner Broadcasting, 512 U.S. at 658.

**3.     Restrictions On Fully Protected Speech Must Be Narrowly Tailored To Serve A Compelling Governmental Interest And Must Be The Least Restrictive Means To Satisfy That Interest.**

A regulation that is subject to strict scrutiny under the First Amendment “rarely survives such scrutiny.” Burson v. Freeman, 504 U.S. 191, 200 (1992). In order to do so, three tests must all be met: (i) the governmental interest served by the restrictions must be compelling, (ii) the restrictions must be narrowly tailored to serve the agency’s stated interests, and (iii) the restrictions must be the least restrictive means of furthering those interests. Sable Communications, 492 U.S. at 126 (“Government may . . . regulate the content of constitutionally protected speech in order to promote a compelling interest if it chooses the least restrictive means to further the articulated interest”); Time Warner Entertainment Co. v. Federal Communications Comm’n, 93 F.3d 957, 966 (D.C. Cir. 1996) (same); Action for Children’s Television v. Federal Communications Comm’n, 58 F.3d 654, 659 (D.C. Cir. 1995) (same), cert. denied, 116 S. Ct. 701 (1996). In other words, the means chosen by the government to further its compelling interests must be “narrowly drawn . . . to serve those interests without unnecessarily interfering with First Amendment freedoms.” Sable Communications, 492 U.S. at 126 (internal quotation marks omitted). It is FDA’s burden to show precisely what interests it seeks to advance. Simon & Schuster, 502 U.S. at 118 (“the State must show that its regulation is necessary to serve a compelling state interest and is narrowly drawn to achieve that end”) (quoting Arkansas Writers’ Project, 481 U.S. at 231).



**4. FDA's Off-Label Speech Restrictions Are Not Narrowly Tailored To Serve A Compelling Governmental Interest.**

Despite the requirements of Simon & Schuster and Arkansas Writers' Project, FDA has not specifically identified what compelling interests its restrictions supposedly are intended to serve. Moreover, with respect to those interests that can be perceived, FDA has not shown -- and cannot show -- that its restrictions advance its goals in the most narrowly tailored fashion. A regulation is "narrowly tailored" in this context only if it is "designed to serve [the government's interests] without unnecessarily interfering with First Amendment freedoms." Sable Communications, 492 U.S. at 126. Because FDA's restrictions on manufacturer speech are based on an almost complete prohibition of speech concerning certain disfavored subjects, they cannot survive review.

The only apparent catalogue of FDA's reasons for restricting manufacturer speech is set forth in the Federal Register Notice belatedly requesting comment on WLF's October 22, 1993 Citizen Petition. There, FDA claims that promotion of off-label uses by manufacturers can (i) "subject patients to unnecessary and dangerous risks," (ii) "encourage physicians and patients to make decisions based on statements or claims that are, in many cases, supported by little or no data," (iii) "place physicians and patients in positions where they cannot make informed, unbiased decision[s]," and (iv) "decrease the incentive of sponsors to conduct well-controlled clinical investigations" necessary for on-label approval. Notice at 59821-22. As discussed below, most of these rationales are illogical on their face, particularly in view of the fact that the speech FDA is attempting to suppress is available to doctors from other sources, without any restrictions being imposed by FDA or any other governmental authority. Even assuming FDA's

stated interests to be both rational and compelling, however, the lack of narrow tailoring -- or, indeed, of any tailoring -- precludes a finding of compliance with the First Amendment.

FDA first claims that “the promotion of unapproved uses by manufacturers [] can subject patients to unnecessary and dangerous risks.” *Id.* at 59821. Even assuming that the dissemination of scientific information can be “promotion,” the invocation of the broad (and universal) goal of patient protection cannot overcome the lack of evidence to support FDA’s claim or the fact that there is no logical link between patient protection and the restrictions at issue. To begin with, any contention that manufacturers’ speech can put patients at risk is illogical because it ignores the fact that the speech is directed to doctors, not patients, and provides those doctors with additional clinical information on which to base their treatment decisions. Thus, the manufacturers’ speech does not “subject” patients to anything.

FDA recognizes that off-label uses are both legal and, on balance, beneficial to patients. *See, e.g.,* Hubbard Tr. 59 (FDA “recognizes and accepts th[e] reality” that off-label uses are often “essential to good medical practice” and in some areas “constitute a significant portion of standard therapy”); *see also supra*, pp. 5-8. FDA also recognizes that patient care is best served when physicians have the fullest possible information about scientific advancements and can therefore make informed judgments concerning individualized treatment regimens. *See, e.g.,* Hubbard Tr. 60; *see also supra*, pp. 9-10. Thus, it is beyond dispute that much of the information that FDA is attempting to suppress is beneficial.

The essentially blanket prohibition on all communications concerning off-label uses cannot be justified on the basis of patient risk because, even to the extent that the restrictions might somehow advance the asserted interest in some cases -- an unproven proposition at best -- the restrictions are not narrowly tailored in any meaningful sense and extend to communications



(e.g., reprints from reputable scientific journals) that cannot be shown to be likely to cause patient harm. On the contrary, it is the withholding of truthful and important scientific information from doctors that is likely to harm patients, because physicians are being deprived of additional, available knowledge concerning important new treatments. See Fox Dec. ¶¶ 6, 10-11; cf. Temple Tr. 72; Hubbard Tr. 60 (important for physicians to have “reliable, up-to-date information regarding off-label uses on which to base their practice decisions”). Indeed, the recent enactment of the FDA reform legislation reflects the Congressional determination that FDA has been overzealous in stifling manufacturers’ communications concerning off label uses.

FDA may well have a legitimate interest in preventing the dissemination of false and misleading information about off-label uses, just as it would have an interest in preventing dissemination of false information concerning on-label uses. However, the First Amendment does not permit prior restraint of a broad category of speech based on the mere possibility that some deceptive or otherwise harmful speech might occur in that context. Ibanez v. Florida Dept. of Business and Professional Regulation, 114 S. Ct. 2084, 2089 (1994) (even in commercial speech context, regulators must distinguish false speech from truthful). Despite this constitutional requirement, FDA makes no effort to distinguish between truthful, beneficial information and whatever information FDA considers harmful. See, e.g., Hubbard Tr. 64-65, 123 (claiming that any promotion of an off-label use is per se false and misleading); Tart Tr. 132-33.

FDA’s second claim, that “[p]romotion of unapproved uses can encourage physicians and patients to make decisions based on statements or claims that are, in many cases, supported by little or no data,” is equally unavailing. Notice at 59821. As noted above, neither the FDA’s regulatory actions (i.e., the Reprint Guidance, Textbook Guidance, and Draft Symposium Order)

nor this challenge concern communications directed to patients. See Reprint Guidance and Textbook Guidance at 52800; Draft Symposium Order at 56412. Thus, FDA's reference to patients' decisions is facially inapposite.

Even insofar as it pertains to the actual audience -- doctors -- FDA's stated rationale provides no support for its policy. It is beyond dispute that doctors are sophisticated professionals. Cf. Hubbard Tr. 54 ("doctors are certainly willing and able to be skeptical of anything"). To the extent that FDA's true concern is that some materials may include statements that are supported by little or no data, FDA cannot reasonably contend that the doctors who receive these materials are incapable of assessing the supporting data and making appropriate judgments. See, e.g., Fox Dec. ¶ 8 (discussing pertinent factors concerning reliability); cf. Hubbard Tr. 121 ("the physician in clinical practice is well-equipped to make responsible, prescribing choices for both approved and unapproved uses"). That is what doctors must do all the time, with respect to both on-label and off-label uses.

Moreover, FDA can point to no proof that the published materials and/or CME presentations at issue are based on insufficiently rigorous studies. Cf. Simon & Schuster, 502 U.S. at 118 (burden on government to prove necessity of restriction). Even assuming that such proof could be adduced, however, it would not support the restrictions at issue here, which are speaker- and content-based and extend far beyond any plausible attempt to ensure the sufficiency of data. For example, FDA bans redistribution of any article unless its principal subject is an on-label use; this is a purely content-based restriction that effectively bars redistribution of articles concerning off-label uses without regard to the quality of the supporting data. Reprint Guidance at 52801. Thus, to the extent that the professed concern about data quality actually motivated these regulations, FDA has not even attempted to tailor its restrictions to meet its stated goal.

WLF does not challenge here the requirements that arguably relate to data quality (e.g., that reprinted articles be from peer-reviewed journals or that textbooks be generally available commercially (rather than being produced solely for distribution by manufacturers). Given this fact, there can be no serious claim that the science at issue here is anything less than rigorous.<sup>13</sup> Indeed, FDA admits that it is entirely appropriate and desirable for physicians to receive and rely on these same materials; its posture changes only when it is manufacturers that seek to redistribute the materials. See, e.g., Hubbard Tr. 62-63 (“it’s very appropriate for physicians to get information about off-label uses from the many sources [from which] they get them . . . . And, of course, they get them from CME; they get them from on-line databases; they get them through textbooks; they get them from discussions with colleagues; they get them from going to a medical center and attending grand rounds.”).

The foregoing discussion applies equally to FDA’s third asserted interest, that manufacturer communications on off-label uses “can place physicians and patients in positions where they cannot make an informed, unbiased decision.” Notice at 59821-22. This is the most illogical of all of FDA’s claimed justifications. It defies reason to contend that additional information cannot be provided to doctors because, if it is, those doctors will be unable to make informed decisions. Indeed, even in contexts where speech receives less stringent protection than it does here, the Supreme Court has repeatedly and emphatically rejected governmental attempts to equate less information with better decision-making. See, e.g., 44 Liquormart, 116 S. Ct. at

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<sup>13</sup> This is not to say that the science may not later be proven wrong. With both on-label and off-label uses, there is the constant possibility that later studies will discover that a drug is not as effective as previously believed or that there are previously unknown side effects. However, as the recent withdrawals of several high-profile FDA-approved drugs emphasize, this phenomenon is not in any way unique to off-label uses.

1505 (“a State’s paternalistic assumption that the public will use truthful, non-misleading commercial information unwisely cannot justify the decision to suppress it.”).

Finally, FDA also has asserted that affording manufacturers greater ability to disseminate information about off-label uses “can also decrease the incentive of sponsors to conduct the well-controlled clinical investigations that are necessary to demonstrate whether the products are safe and effective for their intended uses.” Notice at 59822. Thus, it appears that FDA is asserting an interest in forcing manufacturers to submit supplemental applications for new uses for previously approved products (*i.e.*, bringing off-label uses on-label).

Even assuming that this is an arguably legitimate interest, it is hardly compelling and cannot justify the broad restrictions at issue here. As discussed above, FDA has admitted that off-label uses are not only beneficial, but inevitable due to regulatory lags and other systemic factors. *See supra*, pp. 7-9. Thus, if the intent is to limit uses to those that are on-label and to prohibit off-label uses, FDA has acknowledged that such a goal is neither desirable nor feasible. In any event, FDA cannot use a speech restriction to pursue these goals. “[S]pecial concerns arise from ‘regulations that entirely suppress commercial speech in order to pursue a non speech-related policy.’” *44 Liquormart*, 116 S. Ct. at 1506. If this is true with respect to commercial speech, it is true *a fortiori* with respect to fully protected speech.

FDA admits that many factors militate against adding new uses to approved labeling, including, *inter alia*, the unavoidable time lapse between scientific discoveries and the submission of an application, the sometimes unjustifiable expense of conducting clinical trials, the substantial delays attendant to agency review of supplemental use applications, and the limited market potential for some beneficial new uses. *See supra*, pp. 7-8. None of these factors is changed by restricting manufacturer dissemination of information. Moreover, while FDA has

initiated some efforts to bring more uses on-label, this effort has not been pursued with the diligence that would suggest a “compelling” interest or need. See Temple Tr. 75-78, 95-97.

Even assuming that all of the relief requested by WLF is granted, there still will be substantial differences in permitted marketing of on-label as opposed to off-label uses (for example, direct sales efforts). Accordingly, there is no basis to conclude that the restrictions at issue will have anything but a marginal effect, at most, on requests for supplemental use approvals. Such marginal and speculative benefits cannot justify a broad restriction on First Amendment rights. See Community for Creative Non-Violence v. Kerrigan, 865 F.2d 382, 390 (D.C. Cir. 1989) (“the court must closely scrutinize the regulation to determine if it indeed promotes the Government’s purposes in more than a speculative way”).

The chilling effects of FDA’s restrictions are exacerbated by the intentionally vague nature of the standards, which give FDA nearly unbridled discretion to restrict scientific speech and provide few, if any, “safe harbors” for communication by manufacturers concerning off-label uses. For example, under the Textbook Guidance, it is FDA that decides whether a manufacturer “significantly influenced” the contents of the book, whether the book focuses “primarily” on a manufacturer’s product(s), whether the book provides “a significant focus” on off-label uses, or whether, in certain circumstances, the book has a sufficiently “balanced presentation” to be permissible. Under the Reprint Guidance, FDA maintains the right to determine matters such as whether the “principal subject” of the reprinted article is an approved use and whether the reprinted article discloses in a sufficiently “prominent” and “specific” manner any “effectiveness rates, data, analyses, uses, regimens, or other information” that differ from FDA-approved labeling. Even these sweeping grants (to itself) of essentially standardless discretion are not enough for FDA -- under both Guidances, FDA warns that the provisions “do[ ] not create or

confer any rights” or “bind FDA in any way.” Reprint Guidance at 52801 n.1; Textbook Guidance at 52801 n.2. Similarly, the contract required under the “safe harbor” provision of the Draft Symposium Order is so subjective as to be unenforceable by a court. Consequently, it affords the agency wide latitude to second-guess content determinations made at CME seminars and similar academic events.

The impact of these measures has been to chill all speech that manufacturers and program providers fear might conceivably be found objectionable by FDA. The Reprint and Textbook Guidances, and the Draft Symposium Order epitomize the kind of discretionary review over content is most repugnant to the core values of the First Amendment. See, e.g., Shuttlesworth v. Birmingham, 394 U.S. 147, 150-51 (1969) (city’s “virtually unbridled and absolute power to prohibit parades unconstitutional for lack of “narrow, objective, and definite standards to guide the licensing authority”); Southeastern Promotions Ltd. v. Conrad, 420 U.S. 546, 553 (1975) (“the danger of censorship and abridgment of our precious First Amendment freedoms is too great where officials have unbridled discretion” over speech); City of Lakewood v. Plain Dealer Publishing Co., 486 U.S. 750, 759-60 (1988) (standardless discretion a “direct threat to speech” when regulatory scheme “allow[s] licensor to view the actual content of the speech to be licensed or permitted”). Accordingly, the restrictions must be struck down because they are not narrowly tailored to serve any compelling governmental purpose.<sup>14</sup>

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<sup>14</sup> The degree of discretion that FDA reserves to itself under the Guidances and Draft Symposium Order also render the restrictions so vague that persons “of common intelligence must necessarily guess at [their] meaning and differ as to [their] application.” Connally v. General Construction Co., 269 U.S. 385, 391 (1926). Vagueness is of particular concern to the Supreme Court where speech restrictions are concerned: “Those . . . sensitive to the perils posed by indefinite language[ ] avoid the risk . . . only by restricting their conduct to that which is unquestionably safe. Free speech may not be so inhibited.” Baggett v. Bullitt, 377 U.S. 360, 372 (continued...)



**5.     The Off-Label Speech Restraints Are Not The Least Restrictive Means Of Serving Any Legitimate Governmental Interest.**

Under the strict scrutiny standard applicable to fully protected scientific speech, FDA's constraints also must be the "least restrictive means" available to serve the intended purposes. See, e.g., Boos, 485 U.S. at 329 (regulation struck down because "a less restrictive alternative is readily available"); see also Sable, 492 U.S. at 129 ("the congressional record contains no legislative findings that would justify us in concluding that there is no constitutionally acceptable less restrictive means"). Because the restrictions at issue here also fail this additional test, they must be invalidated.

At the outset, there is a serious question as to whether any prior restraint of the type imposed by the regulations at issue here is necessary or appropriate in view of the vast post-dissemination powers that are available to FDA and that may be targeted against any actually false or misleading statements. For example, in the event that a manufacturer makes a false statement concerning one of its products, FDA has the authority, among other remedies, to enjoin distribution or even to seize all of the product. 21 U.S.C. §§ 303-04. In such a situation, the manufacturer also could be subject to criminal penalties. 21 U.S.C. §§ 301, 303. These enforcement powers provide appropriate incentives against dissemination of any actually false or misleading materials, while not simultaneously prohibiting beneficial speech. As such, these powers represent less restrictive alternatives that are available to FDA and are already in place.

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(...continued)

(1964); see also, e.g., Gentile v. State Bar of Nevada, 501 U.S. 1030 (1991) (state bar restriction on "extrajudicial" speech void for vagueness).



FDA also has stated that it has additional powers that may be exercised if FDA has concerns about some particular off-label use. FDA specifically has asserted authority under the FDCA to place post-marketing restrictions on approved drugs. See 21 C.F.R. § 314.520. This provision provides:

(a) If FDA concludes that a drug product shown to be effective can be safely used only if distribution or use is restricted, FDA will require such postmarketing restrictions as are needed to assure safe use of the drug product, such as:

(1) Distribution restricted to certain facilities or physicians with special training or experience; or

(2) Distribution conditioned on the performance of specified medical procedures.

(b) The limitations imposed will be commensurate with the specific safety concerns presented by the drug product.

In connection with the adoption of 21 C.F.R. § 314.520, FDA stated that:

There is no legal support for the theory that FDA may only approve sponsors' drugs without restriction because physicians or pharmacists may wish to prescribe or dispense drugs in a certain way. The restrictions under these provisions would be imposed on the sponsor only as necessary for safe use under the extraordinary circumstances of the particular drug and use. Without such restrictions, the drugs would not meet the statutory criteria, could not be approved for distribution, and would not be available for prescribing or dispensing. The agency, as a matter of long-standing policy, does not wish to interfere with the practice of medicine or pharmacy. In this instance, the agency believes that rather than interfering with physician or pharmacy practice, the regulations permit, in exceptional cases, approval of drugs with restrictions so that the drugs may be available for prescribing or dispensing.

57 Fed. Reg. 58942, 58951-52 (Dec. 11, 1992). Thus, FDA has non-speech powers that are capable of directly serving the goals asserted for FDA's speech-related restrictions, without infringing on the doctors' or manufacturers' First Amendment rights.

Finally, to the extent that any speech-based restrictions are necessary or appropriate in the context of the speech at issue here -- manufacturer-supported distribution of scientific data and information to physicians and other sophisticated professionals -- mandatory disclosures provide a less restrictive but still effective means to serve any legitimate interests. For purposes of this case, WLF does not object to any required disclosure that (i) the speech concerns off-label uses and (ii) a financially interested manufacturer has provided or otherwise supported the dissemination. It is undisputed that the receiving audience -- physicians and other health care professionals -- is knowledgeable about the process of scientific debate and the testing of medical hypotheses. See Hubbard Tr. 54 ("doctors are certainly willing and able to be skeptical of anything"), 56-57 (doctors themselves not asking for limitation on information but want to know "if we are being promoted to" and "that it is the drug company talking to us"); Fox Dec. ¶ 8 ("I have little difficulty in separating articles that I deem highly reliable from those with lesser reliability"). Many physicians have indicated that such disclosures are sufficient to aid them in making reasoned judgments about the content of the communications. See, e.g., Hubbard Tr. 56-57; Fox. Dec. ¶¶ 7-8. Particularly in view of FDA's vast post-speech and non-speech powers, advance disclosure of any manufacturer interest and of the fact that the speech concerns an off-label use will sufficiently protect any legitimate interests that FDA may have. Consequently, FDA's elaborate and intrusive scheme banning essentially all manufacturer speech is constitutionally impermissible and must be struck down.

**D. At A Minimum, FDA's Enforcement Policies Unconstitutionally Restrict Protected Commercial Speech.**

Although the government has greater leeway to regulate commercial speech, putative regulators of such speech still face a significant burden. At a minimum, the Supreme Court requires that the government prove that the restriction "directly advances" a "substantial interest" and is "narrowly tailored" to achieve a reasonable "fit" between FDA's stated goals and the agency's means of achieving them. Central Hudson, 447 U.S. at 557; Fox, 492 U.S. at 480. For the Central Hudson test to be satisfied, the Court must be persuaded that the cost of the regulation has been "carefully calculated." Discovery Network, 507 U.S. at 416 n.12. As with fully protected speech, the burden of justifying its restriction rests squarely on FDA. Bolger, 463 U.S. at 71 n.20 ("party seeking to uphold a restriction on commercial speech carries the burden of justifying it"). Further, blanket bans on commercial speech are as disfavored under the Supreme Court's jurisprudence as are prophylactic bans on fully protected speech. See 44 Liquormart, 116 S. Ct. at 1507-08.

**1. The Speech At Issue Concerns Lawful Activity And Is Not Misleading.**

To qualify for constitutional protection, commercial speech first "must concern lawful activity and not be misleading." Central Hudson, 447 U.S. at 566. FDA does not dispute that off-label uses are lawful activities that are neither regulated nor prohibited by FDA. Hubbard Tr. 60, 121, 124, 142, 147; Tart Tr. 28. Indeed, FDA admits that off-label uses are proper and often represent the state of the art in practice. Hubbard Tr. 59; Tart Tr. 159; Temple Tr. 71.

Any suggestion that FDA may nonetheless severely constrain manufacturer speech on off-label uses because any manufacturer participation in such discussions is per se misleading -- which is the sweeping proposition that would be necessary to support the pervasive restrictions here -- is untenable both legally and as a matter of fact. The Supreme Court has made clear that the "free flow of commercial information is valuable enough to justify imposing on would-be regulators the costs of distinguishing the truthful from the false, the helpful from the misleading, and the harmless from the harmful." Ibanez, 114 S. Ct. at 2089 (quoting Zauderer v. Office of Disciplinary Counsel of Supreme Court of Ohio, 471 U.S. 626, 646 (1985)). The precedents do not allow "rote invocation of the words 'potentially misleading' to supplant the [government's] burden" of proving that the speech is in fact misleading. Ibanez, 114 S. Ct. at 2090.

No proof that the communications are actually misleading is possible here. FDA has not shown, as it must, that manufacturers will frequently use the mechanisms at issue here -- circulation of reprints of peer-reviewed journal articles or textbooks and sponsorship of CME symposia -- to discuss or promote off-label uses that are inconsistent with the scientific evidence. Indeed, any such assumption is belied by FDA's admitted practice of allowing manufacturers to respond to unsolicited inquiries concerning off-label uses by providing the same information to an inquiring physician that those manufacturers could not provide absent the inquiry. See Notice at 59823 ("companies may also disseminate information on unapproved uses in response to unsolicited requests for scientific information from health care professionals").

FDA also has no basis for any assumption that authors (who are scientists and researchers), publishers, and symposium organizers would surrender or debase their professional judgment. Authors, publishers, and symposium organizers depend upon their reputations for scientific independence and professionalism to attract the patronage of highly intelligent and

critical audiences. Pre-existing private mechanisms in place, including peer review procedures and independent accreditation standards, work to ensure that written materials and symposia presentations reflect rigorous science. FDA acknowledges as much by relying upon peer review and private accreditation mechanisms to satisfy certain of the agency's requirements. See Reprint Guidance at 52801; Draft Symposium Order at 56413. WLF does not here challenge these aspects of FDA's regulatory policies.

In short, if it wishes to regulate commercial speech on the basis that the speech may be false or misleading, FDA is constitutionally compelled to make particularized fact-based determinations rather than relying on broad unfounded assumptions. FDA has failed to do so.

**2. The Governmental Interests Are No Different -- And No More Substantial -- In The Commercial Speech Context Than In The Non-Commercial Speech Context.**

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As with fully protected speech, FDA must articulate legitimate governmental goals to justify restrictions on commercial speech. The only variation between the two legal analyses is one of degree: restrictions on non-commercial speech must serve a "compelling" state interest, while commercial speech restrictions can be justified if they serve a "substantial" state interest. Sable Communications, 492 U.S. at 126 ("Government may . . . regulate the content of constitutionally protected speech in order to promote a compelling interest if it chooses the least restrictive means to further the articulated interest"); Central Hudson, 447 U.S. at 564 ("State must assert a substantial interest to be achieved by restrictions on commercial speech").

Here, this distinction is without a difference. Any assertion of a general patient protection interest is no more "substantial" than it is "compelling" in view of FDA's admissions that off-label uses are necessary and beneficial and that doctors need information concerning

such uses. See supra, pp. 5-10. FDA's assertion that its restrictions serve generally to force uses "on-label" may encompass a significant FDA interest. However, the Guidances and Draft Symposium Order do not in fact advance that goal. See supra, pp. 28-33. Moreover, FDA's other admissions reveal that the restrictions cannot satisfy any such goal because so many circumstances unrelated to manufacturer promotion affect whether a use is put "on-label." See supra, pp. 7-9. Finally, should FDA's true goal be indirectly to eliminate or restrict physicians' practice of prescribing drugs and devices for off-label uses, the Supreme Court's commercial speech decisions make clear that such a goal is constitutionally impermissible. See 44 Liquormart, 116 S. Ct. at 1506 ("special concerns arise from regulations that entirely suppress commercial speech in order to pursue a non speech-related policy") (internal citations omitted); Central Hudson, 447 U.S. at 570; Linmark Associates, 431 U.S. at 95-96 (rationale for commercial speech restriction less persuasive when restriction strikes at the substance of the information communicated rather than at the commercial transaction).

**3. The Restrictions At Issue Do Not Directly Advance The Governmental Interests Asserted.**

Commercial speech restrictions cannot survive First Amendment scrutiny unless they advance the government's interest in "a direct and material way." Edenfield, 113 S. Ct. at 1798. The Supreme Court has emphasized that this requirement cannot be satisfied with mere speculation and conjecture. Rather, the burden is on FDA to "demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree." Coors, 514 U.S. at 486 (internal quotation marks omitted). A commercial speech regulation "may not be sustained if it provides only ineffective or remote support for the government's purpose."



44 Liquormart, 116 S. Ct. at 1509 (quoting Central Hudson, 447 U.S. at 564); see also Adolph Coors Co. v. Bentsen, 2 F.3d 355, 357 (10th Cir. 1993) (“[i]f the means-end connection is tenuous or highly speculative, the regulation cannot survive constitutional scrutiny”) (internal quotation marks omitted), aff’d sub nom. Rubin v. Coors Brewing Co., 514 U.S. 476 (1995).

As previously demonstrated, the Guidances and Draft Symposium Order do not directly or materially advance FDA’s asserted interests. See supra, pp. 28-33. To sum up briefly, the restrictions on manufacturers’ speech concerning off-label uses do not directly advance any goal of consumer or patient protection because the speech is directed to physicians who then make treatment decisions on the basis of all available information; patients could not act unilaterally on the speech even if the information were somehow to become available to them. See supra, p. 28. The restrictions certainly do not materially advance any goal of helping physicians make informed and unbiased decisions about treatments; on the contrary, allowing manufacturers to provide information simply makes more information more accessible. See supra, pp. 29-32. FDA’s restraints serve only to keep in the dark those physicians who do not receive the information through some other channel -- or who do not happen to make a direct inquiry to the manufacturer. Accordingly, FDA’s restrictions “cannot directly and materially advance its asserted interest[s] because of the overall irrationality of the Government’s regulatory scheme.” Coors, 514 U.S. at 488. Even FDA itself tacitly concedes that the off-label restrictions do not serve to assuage the various factors that may operate to discourage manufacturers from seeking to add new on-label uses for their drugs or devices. See supra, pp. 7-9.

Furthermore, because the Guidances and Draft Symposium Order operate as a blanket ban on manufacturer speech about off-label uses, the restrictions provide no balance between FDA’s legitimate interest in avoiding the spread of false information and the public interest to be



served by promoting a free flow of important data. The cost of the FDA's policy is not "in proportion to the interest served." Fox, 492 U.S. at 480. Instead, the restrictions may be affirmatively harmful. They impede the flow of information about new uses of prescription drugs and devices that may alleviate pain, bolster the health, or even save the lives of many patients. Moreover, the restrictions do so by blocking information from the entities that may well have the most comprehensive information, as FDA acknowledges, see Notice at 59823 ("[s]cientific departments within regulated companies generally maintain a large body of information on their products"), and that often have the greatest incentive to make the information available.

**4.     The Restrictions At Issue Are Far More Extensive Than Necessary To Protect Any Legitimate Governmental Interest.**

Finally, FDA's restrictions are considerably more extensive than necessary to serve -- indeed, they are at odds with -- the only justifiable governmental interest here: helping physicians make informed decisions that can serve individual patient needs. While commercial speech jurisprudence does not require FDA to employ the least restrictive means of advancing an interest, the FDA must make an effort to reasonably fit its means to its ends. 44 Liquormart, 116 S. Ct. at 1510; Discovery Network, 507 U.S. at 416; Edenfield, 507 U.S. at 769; Fox, 492 U.S. at 480. Several facts demonstrate that FDA has failed to do so here.

First, FDA's restrictions are impermissibly broad because they preclude manufacturer-sponsored dissemination of speech concerning off-label uses, even where there are clear indicia

of scientific accuracy and truthfulness.<sup>15</sup> The agency cannot avoid its constitutional obligation to develop tailored restrictions by limiting physicians' access to information that other physicians and scientists believe is important enough to be published.

Furthermore, the availability of other options "which could advance the government's asserted interest[s] in a manner less intrusive to . . . First Amendment rights" serves as another indication that the FDA restrictions are more extensive than necessary. Coors, 514 U.S. at 489-491. As discussed above, in the unlikely event that any manufacturer's activities (i.e., distribution of textbooks or peer-reviewed articles or support of symposia) give rise to any actual and identifiable abuses involving false or misleading information, FDA has more than sufficient enforcement authority to address concrete problems. In addition, the FDA has specifically asserted authority to impose additional limitations on drugs that raise special safety concerns. See supra, pp. 35-37. These powers constitute in-place, non-speech, and less restrictive alternatives to achieve FDA's stated goals.

To the extent that any speech-related restrictions are necessary, disclosure requirements -- mandating conspicuous notifications that the uses under discussion are off-label and that the manufacturer of the product discussed has supported dissemination of the speech -- would be sufficient. See supra, pp. 37-38. Such disclosures would adequately alert physicians to relevant considerations to be weighed in evaluating what action, if any, to take in response to the speech

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<sup>15</sup> FDA cannot use the availability of this information through alternate means to justify its restrictions on manufacturer participation in the broader distribution of the speech. Restrictions on the free flow of information of truthful, non-misleading information cannot stand simply because there is a possibility that other media could convey the same message. See, e.g., Ladue v. Gilleo, 114 S. Ct. 2038 (1994); Bolger, 463 U.S. at 69; Schneider v. State, 308 U.S. 147, 163 (1939).

and would comport well with the general "constitutional presumption favoring disclosure over concealment." Peel v. Attorney Discipline Comm., 496 U.S. 91, 111 (1990).

#### IV. CONCLUSION

For the foregoing reasons, the Court should grant summary judgment in favor of WLF, declare the impermissible aspects of FDA's enforcement policies and regulations to be unlawful and in violation of the First Amendment, and enjoin further enforcement of those policies and guidances. A proposed Order specifying these matters in greater detail is submitted herewith.

Respectfully submitted,

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**CERTIFICATE OF SERVICE**

I hereby certify that on this 24th day of November 1997, I caused copies of the foregoing Memorandum in Support of Plaintiff's Motion for Summary Judgment to be mailed via first-class postage prepaid mail to the following:

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