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NOTES

THE IMPACT OF THE *WASHINGTON LEGAL FOUNDATION* CASES ON PHARMACEUTICAL MANUFACTURER PRACTICES IN THE UNITED STATES

RICHARD C. ASCROFT*

INTRODUCTION

Pharmaceutical manufacturers spend billions of dollars each year on promotional activities.¹ Until recently, the kind of information that a company sales representative could share with healthcare providers was restricted to data on Food and Drug Administration (FDA)-approved uses of a product. However, on July 30, 1998, the U.S. District Court for the District of Columbia held in *Washington Legal Foundation v. Friedman* (WLF I) that the FDA's policies and guidelines restricting the ability of pharmaceutical manufacturers to distribute certain types of "off-label" information for additional uses of already-approved products to healthcare professionals were unconstitutional restraints on speech.² On July 28, 1999, the same court held in *Washington Legal Foundation v. Henney* (WLF II) that its earlier decision also applied to Section 401 of the recently enacted Food and Drug Administration Modernization Act of 1997

* J.D. Candidate, 2001, Indiana University School of Law—Indianapolis; B.S., Pharmacy, 1993, Butler University, Indianapolis, Indiana. The author is a registered pharmacist and Manager of Clinical Operations for New Antidepressant Development at Eli Lilly and Company, Indianapolis, Indiana. The author is not a part of Eli Lilly and Company's Legal Division and has not been involved in either the commercial or clinical development of Evista® (raloxifene hydrochloride). Additionally, the views and opinions of the author are his own and do not necessarily reflect those of Eli Lilly and Company.

1. One of the world's largest pharmaceutical manufacturers, based on IMS Health, is Merck & Co., which spent approximately \$4.5 billion on sales and marketing activities in 1998. See 1998 ANNUAL REPORT FOR MERCK & CO., at <http://www.merck.com.overview/98ar/>. Examples of manufacturer promotional activities include detailing (discussions with healthcare professionals) done by company sales personnel, placing advertisements in industry and medical journals, providing healthcare professionals with printed information on company products, and direct-to-consumer advertising. See, e.g., Lars Noah, *Death of a Salesman: To What Extent Can the FDA Regulate the Promotional Statements of Pharmaceutical Sales Representatives?*, 47 FOOD & DRUG L.J. 309, 311-12 (1992).

2. *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 74 (D.D.C. 1998), appeal dismissed, vacated in part, 202 F.3d 331 (D.C. Cir. 2000).

(FDAMA), which outlined the terms under which pharmaceutical manufacturers would be permitted to disseminate off-label information.³ The FDA appealed both decisions and on February 11, 2000, the U.S. Court of Appeals for the District of Columbia Circuit decided the case⁴ with each side interpreting the court's ruling differently and both sides declaring victory.⁵

Off-label information is information not contained in a product's FDA-approved labeling and, as such, information that has not necessarily received a rigorous review by the agency.⁶ Prior to these holdings, the FDA placed significant hurdles in front of companies that wanted to disseminate off-label information about unapproved uses of drugs to healthcare professionals.⁷ While the FDAMA purported to lessen these restrictions, significant pre-dissemination requirements contained therein prevent much of the available information on unapproved uses of drugs from being shared with healthcare professionals.⁸ Interestingly, the FDA does not restrict physicians from prescribing drugs for unapproved uses, nor does it prevent manufacturers from providing information

3. *Washington Legal Found. v. Henney*, 56 F. Supp. 2d 81, 88 (D.D.C. 1999), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000).

4. *See* *Washington Legal Found. v. Henney*, 202 F.3d 331 (D.C. Cir. 2000).

5. *See* Lisa Richwine, *USA: Court Dismisses FDA Appeal on Drug Promotion*, REUTERS ENG. NEWS SERV., Feb. 11, 2000. "The bottom line of the case is that the provision that Congress passed in FDAMA [the Food and Drug Administration Modernization Act] stays in effect." *Id.* (quoting an FDA official). "The Washington Legal Foundation (WLF) won a major victory today in its long-running battle against Food and Drug Administration (FDA) speech restrictions. . . . [The] 'FDA no longer will be permitted to ban speech about off-label uses of drugs unless it has real reason to believe that the information is false.'" Press Release, Washington Legal Foundation, Appeals Court Affirms Injunction Against FDA Speech Restrictions (Feb. 11, 2000) (quoting Richard Samp, WLF Chief Counsel) (on file with author). The decision has also confused those not associated with the case. "It is not clear whether this is a return to the situation that existed before or whether FDA has a burden to show more than dissemination of information' to bring action against a company." Richwine, *supra*. *See also* discussion *infra* Part IV.

6. According to federal regulations, prescription drug labeling must "contain a summary of the essential scientific information needed for the safe and effective use of the drug." 21 C.F.R. § 201.56(a) (2000). Whenever possible the information contained within the label should be based on "data derived from human experience." 21 C.F.R. § 201.56(c). The label contains information on the following: clinical pharmacology, indications and usage, contraindications, warnings, precautions, adverse reactions, drug abuse and dependence, overdose, dosage and administration, and how the drug is supplied. 21 C.F.R. § 201.56(d)(1). *See also* Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA. L. REV. 181, 187-88 (1999) (defining off-label, off-label use, off-label prescription, and off-label promotion and marketing).

7. *See* Jeffrey N. Gibbs, *First Amendment Limits on Regulating Information: An Initial Reaction to the Washington Legal Foundation Case*, 53 FOOD & DRUG L.J. 597, 597 (1998).

8. *See* Anne Marie Murphy, "It's Time to Make a Good Agency Better": *The Food and Drug Administration Modernization Act of 1997 and the First Amendment*, 53 FOOD & DRUG L.J. 603, 603-04 (1998).

on unapproved uses in response to unsolicited questions.⁹

For proponents of allowing less restrictive dissemination of off-label information, WLF I and II are very encouraging. These proponents contend that the dissemination of off-label information by pharmaceutical companies will benefit society by making medical professionals quickly aware of effective new uses of older treatments.¹⁰ For opponents of this practice, WLF I and II represent a setback. Opponents favor strict FDA control and contend that allowing manufacturers to disseminate off-label information to medical professionals will adversely affect society because the data being shared has not been subjected to the same rigorous review as the data upon which an FDA-approved use is based.¹¹ The FDA also supports this position.¹² This issue is obviously important to pharmaceutical manufacturers who will likely benefit economically if allowed to disseminate off-label information and thereby increase utilization of their products in new markets. It is also important to doctors and patients because of the length of time it takes manufacturers to conduct clinical trials testing for new uses¹³ and for the FDA to approve new uses for already-approved drugs.¹⁴

This Note will explore the impact of the *Washington Legal Foundation Cases* on pharmaceutical manufacturer practices in the United States. Part I will

9. See Linda A. Suydam, Keynote Address for FDLI Conference on Advertising and Promotion in the New Millennium 5-6 (Sept. 13, 1999), at <http://www.fda.gov/OC/speeches/offlabel.html>. The FDA acknowledges that “the legislative history of the Federal Food, Drug, and Cosmetic Act shows that Congress did not intend FDA to interfere with the practice of medicine, and FDA . . . has never had such a goal.” *Id.* at 2. Additionally, the FDA does not want to control the publication of scientific data and does not prohibit a manufacturer from sharing off-label information that has been requested by a medical doctor. *See id.* at 6. Instead, the FDA’s concern is promotion of off-label information by pharmaceutical manufacturers. *See id.*

10. See Salbu, *supra* note 6, at 193-95.

11. *See id.* at 201-10.

12. *See* Washington Legal Found. v. Friedman, 13 F. Supp. 51, 57 (D.D.C. 1998), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000).

13. A study conducted at the Tuft’s Center for the Study of Drug Development showed that the average clinical development time for new drugs approved by the FDA between 1996-1998 was 5.9 years. *See* FDA OFFICE OF PLANNING, *Fiscal Year 1999 Performance Report to Congress for the Prescription Drug User Fee Act of 1992* (Food and Drug Administration, Rockville, MD), 1999, at <http://www.fda.gov/ope/pdufa/report99/default.html> [hereinafter *1999 Performance Report*]. However, a manufacturer may be allowed to do less clinical development for a new use resulting in a slight reduction in development time. *See* MARK MATHIEU, *NEW DRUG DEVELOPMENT: A REGULATORY OVERVIEW* 293 (Parexel Int’l Corp., 4th ed. 1997).

14. In 1998, the median FDA-approval time for new or expanded uses for already-approved drugs was 11.8 months. *See Improving Public Health Through Human Drugs*, CDER 1998 REPORT TO THE NATION (Food and Drug Administration, Rockville, MD), 1998, at 10, <http://www.fda.gov/cder/reports/rptntn98.pdf>. In 1999, the FDA reviewed and acted upon ninety percent of efficacy supplements (supplements for new uses) within twelve months. *See 1999 Performance Report*, *supra* note 13.

define off-label information and provide an overview of the arguments for and against the dissemination of this information by pharmaceutical companies. Part II will provide relevant background on the restrictions placed on pharmaceutical companies by the FDA prior to the holdings in WLF I and II. Part III will discuss the procedural history of the *Washington Legal Foundation Cases* and fully review the framework established by Judge Royce C. Lamberth in WLF I regarding dissemination of off-label information by pharmaceutical companies. This part will also review the U.S. Court of Appeals' recent decision. Part IV will posit that other factors, beyond FDA intervention, protect both consumers and competitors from the purported harms associated with pharmaceutical company dissemination of off-label information. In addressing these factors, which include product liability claims, civil suits by other manufacturers under the Lanham Act, and the realities of the pharmaceutical marketplace, this part will delve into the relevant areas of law. Additionally, uncertainties created by the decisions in WLF I, WLF II, and the recent U.S. Court of Appeals' decision will be discussed. Part V will argue that the framework established by WLF I, when combined with product liability laws, the Lanham Act, and the pressures of the pharmaceutical market, create an environment permitting the dissemination of off-label information by manufacturers, while still providing adequate protection for society, but only if existing uncertainties are resolved. Finally, this part will suggest potential solutions to the existing uncertainties.

I. DISSEMINATION OF OFF-LABEL INFORMATION BY PHARMACEUTICAL COMPANIES: ARGUMENTS FOR AND AGAINST

In the United States, off-label information is, by definition, information that is not included in a drug's FDA-approved package insert.¹⁵ The package insert is proposed by the pharmaceutical manufacturer and approved by the FDA when the new drug or new use for an already-marketed drug is evaluated.¹⁶ Therefore, off-label information generally has not received the rigorous review required for approval of a product or a new use. It is not disputed either that physicians should be able to prescribe drugs for off-label use or that information about off-label uses can be published.¹⁷ The controversy surrounding off-label information centers upon whether pharmaceutical manufacturers should be allowed to disseminate this information about new uses of already approved products to healthcare professionals.¹⁸ Arguments exist both favoring and disfavoring

15. See discussion *supra* note 6. Because of the large amount of information required to be included in a prescription drug label, it is difficult for a manufacturer to place the information on a product's immediate container. Therefore, manufacturers include the information in a package insert that is affixed to the drug's container or packaging. See MATHIEU, *supra* note 13, at 224-25; see also Salbu, *supra* note 6, at 187.

16. Approval of a prescription drug's package insert is usually the last step in the FDA's drug approval process. See MATHIEU, *supra* note 13, at 223.

17. See Suydam, *supra* note 9, at 5-6.

18. See Salbu, *supra* note 6, at 191-92.

pharmaceutical manufacturer dissemination of off-label information.

A. Arguments For the Dissemination of Off-Label Information

Proponents for a more open policy on the dissemination of off-label information argue that because the practice of prescribing drugs off-label is prevalent, information should be readily available to help physicians make informed decisions.¹⁹ Although the exact number is disputed, between twenty and sixty percent of prescriptions are for off-label uses.²⁰ The FDA recognizes that prescribing drugs for off-label uses can be beneficial and does not regulate the activity.²¹ Moreover, because physicians receive a large amount of information from pharmaceutical sales representatives,²² placing restrictions on manufacturer dissemination of off-label information may lead to patients not receiving optimal treatments.

In addition, much of today's medical research is funded by the pharmaceutical industry. Proponents argue that manufacturers have the greatest resources and incentive to share the latest information with healthcare professionals.²³ While the FDA's review process for new product uses has improved, FDA approval still lags behind the availability of the most innovative approaches and therapies.²⁴ Thus, preventing pharmaceutical manufacturers from disseminating off-label information until new uses are approved hampers one of the key avenues for sharing information with the largest number of physicians. Additionally, proponents argue that physicians are highly educated and well-equipped to read a peer-reviewed article and make sound medical decisions on the basis of published data, regardless of the data's source.²⁵ As the court noted in WLF I, "[w]hy the ability of a doctor to critically evaluate scientific findings depends upon how the article got into a physician's hands . . . is unclear to this court."²⁶

19. See *id.* at 193-95.

20. See *id.* at 193; *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 56 (D.D.C. 1998), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000). In some therapeutic areas, like oncology, off-label use is often considered to be state-of-the art treatment. See Gail Dutton, *Should You Let the FDA Decide What Drugs You Pay For?*, BUS. & HEALTH, Oct. 1, 1996, at 65.

21. See *Suydam*, *supra* note 9, at 2.

22. See *Noah*, *supra* note 1, at 311-12.

23. See *Salbu*, *supra* note 6, at 198-99.

24. See Nancy K. Plant, *Prescription Drug Promotion on the Internet: Tool for the Inquisitive or Trap for the Unwary?*, 42 ST. LOUIS U. L.J. 89, 97 (1998); see also discussion *supra* note 14.

25. See *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 70 (D.D.C. 1998), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000).

26. *Id.*

B. Arguments Against the Dissemination of Off-Label Information

Opponents of off-label dissemination by manufacturers contend that instead of helping society, this practice is harmful.²⁷ They favor more involvement by the FDA and feel that the only way to protect society is via the FDA's rigorous review and approval process.²⁸ This is the view advanced by the FDA.²⁹ Opponents cite examples of where the latest medical breakthroughs published in a peer-reviewed journal either turn out to be wrong or were actually harmful to patients.³⁰ They also contend that new uses of drugs are not significantly different from experimental new drugs and, as such, should go through the same thorough review and approval process.³¹

In addition, opponents fear that pharmaceutical manufacturers will no longer have any incentives to complete the necessary studies to receive FDA approval for new uses of their products.³² They also fear that pharmaceutical manufacturers will not provide a fair, balanced review of information to physicians when they discuss off-label uses.³³ Because pharmaceutical companies are in the business of making money on their products, the fear exists that they will have little incentive to discuss their products' risks or the results of other studies with adverse or contrary findings.³⁴ They further contend that the FDA does not restrict the publication of off-label uses and that physicians are able to access this information through textbooks, on-line databases, peer-review journals, and continuing education programs.³⁵

II. THE REGULATORY/LEGAL ENVIRONMENT PRIOR TO WLF

The FDA has the authority to regulate the labeling and advertising of prescription pharmaceuticals under the Federal Food, Drug, and Cosmetic Act (FDCA).³⁶ Labeling is broader than just the label on the bottle; it also includes the product's package insert and all promotional materials including the detailing brochures used by the manufacturer to promote sales of the product.³⁷ Under the

27. See Salbu, *supra* note 6, at 201.

28. See Suydam, *supra* note 9, at 1.

29. See *id.*

30. See *id.* at 4. These examples include significant cardiovascular problems arising from using the combination of fenfluramine and phentermine off-label for weight-loss, and the increased mortality associated with the off-label use of the anti-arrhythmic drugs, encainide and flecainide, in certain heart attack patients that was thought to decrease mortality. See *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 56 (D.D.C. 1998); *American Home Products Corp. Settles Wrongful-Death Suit Over a Diet Drug*, WALL ST. J., June 23, 1999, at B17.

31. See Salbu, *supra* note 6, at 204.

32. See Suydam, *supra* note 9, at 2.

33. See Salbu, *supra* note 6, at 206-07.

34. See *id.*

35. See Suydam, *supra* note 9, at 2.

36. 21 U.S.C. §§ 301, 393 (1999).

37. See 21 C.F.R. § 202.1(1)(2) (1996).

FDCA, the FDA must use the formal rule making process to promulgate regulations.³⁸ However, the FDA often avoids the formal rule making process outlined in the Act by producing Guidance Documents, which, while not binding on the FDA or the industry, are generally followed by the industry.³⁹

On October 8, 1996, the FDA published two Guidance Documents concerning the dissemination of data from medical and scientific textbooks and reprints of articles from scientific and medical journals.⁴⁰ With regard to reprints of scientific and medical journals, the Guidance Documents required that the “principal subject of the article should be the use(s) or indication(s) that has been approved by the FDA.”⁴¹ They further required that “[t]he reprint should be from a bona fide peer-reviewed journal” and if the article contained information that differed from the FDA-approved prescription drug label “the reprint should prominently state the difference(s), with specificity, on the face of the reprint.”⁴² With regard to textbooks, the Guidance Documents required that the textbook should not have been written or published specifically for a manufacturer or reviewed or edited or significantly influenced by a manufacturer.⁴³ Additionally, the text “should not be distributed only or primarily through drug, device, or biologic firms” and the text should not focus on the disseminating company’s particular product(s).⁴⁴ Finally, commenting on the off-label information that is often contained in such medical articles, the Guidance Documents stated that the text should not have a “significant focus on unapproved uses of the drug(s), device(s), or biologic(s) marketed or under investigation by the firm supporting the dissemination of the text.”⁴⁵

Prior to the 1997 passage of the FDAMA, the FDA strongly opposed the dissemination of off-label information by a manufacturer. The agency and at least one U.S. Attorney deemed the activity appropriate for criminal enforcement.⁴⁶ The FDAMA represented the first significant change to the

38. See 21 U.S.C.A § 371 (1999).

39. See *id.* § 371(h)(1)(a); Plant, *supra* note 24, at 93.

Although guidance documents cannot legally bind FDA or the public, the agency recognizes the value of guidance documents in providing consistency and predictability. A company wants assurance that if it chooses to follow a guidance document, FDA generally will find it to be in compliance with the statute and regulations. . . . With these principles in mind, FDA’s decisionmakers will take steps to ensure that their staff do not deviate from guidance documents without appropriate justification and without first obtaining concurrence from a supervisor.

Food and Drug Administration’s Development, Issuance, and Use of Guidance Documents, 62 Fed. Reg. 8961, 8963 (Feb. 27, 1997).

40. See Advertising and Promotion; Guidances, 61 Fed. Reg. 52800 (Oct. 8, 1996).

41. *Id.* at 52801.

42. *Id.*

43. See *id.*

44. *Id.*

45. *Id.*

46. See 1. Scott Bass et al., *Off-Label Promotion: Is FDA’s Final Guidance on Industry-*

FDCA since 1962.⁴⁷

The FDAMA contained numerous revisions to the FDCA, including section 401, a provision which, for the first time, allowed pharmaceutical manufacturers to disseminate off-label information under certain circumstances.⁴⁸ One such requirement under the FDAMA is the dissemination to certain groups only: health care practitioners, pharmacy benefit managers, health insurance issuers, group health plans, and governmental agencies.⁴⁹ Additionally, under the FDAMA, manufacturers can only disseminate authorized information contained in either unabridged peer-reviewed articles or certain qualified reference publications.⁵⁰ Also, the information cannot derive from research conducted by another manufacturer unless that manufacturer provides permission to disseminate the information.⁵¹ At least sixty days prior to the dissemination, the manufacturer must submit the information to the Secretary of Health and Human Services and provide any additional safety and efficacy data the manufacturer has on the product.⁵² Most importantly, under the FDAMA, manufacturers can only disseminate off-label information if either they are actively pursuing FDA approval to market the new use or the pursuit of such approval would be cost-prohibitive or unethical.⁵³

When manufacturers disseminate off-label information, they must prominently affix to the information a disclaimer that the information concerns a use of a drug or device that has not been approved by the FDA and, if applicable, that other drugs are approved for this use.⁵⁴ Manufacturers must also identify how the research was funded and any affiliations between the authors

Supported Scientific and Educational Programs Enforceable?, 53 FOOD & DRUG L.J. 193, 193-94 (1998). The actual offense or charge against the pharmaceutical company would be "misbranding" under 21 U.S.C.A. § 331(b) (1999). A product is misbranded if its labeling or advertising do not comport with the FDCA. See 21 U.S.C.A. § 352 (1999). Penalties for misbranding and other violations of section 331 are set forth in section 333(a), "[a]ny person who violates a provision of section 331 of this title shall be imprisoned for not more than one year or fined not more than \$1,000, or both." *Id.* § 333(a)(1).

47. See Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (1997) (codified as amended in scattered sections of 21 U.S.C.A. § 301 (2000)).

48. See 21 U.S.C.A. § 360aaa-6.

49. See *id.* § 360aaa(a).

50. See *id.* § 360aaa-1.

51. See *id.* § 360aaa(b)(3).

52. See *id.* § 360aaa(b)(4).

53. See *id.* § 360aaa-3. The vehicle by which a drug sponsor, or pharmaceutical company formally asks the FDA to approve the sale of a new pharmaceutical is the New Drug Application (NDA). See MATHIEU, *supra* note 13, at 165. Once a company has its product approved for sale by the FDA, the company "can access and 'supplement' the [original] application's data to seek FDA authorization to market variations of the drug beyond those provided for in the approved NDA." *Id.* at 283. This supplement is called a Supplemental NDA (sNDA).

54. See 21 U.S.C.A. § 360aaa(b)(6) (1999).

and the disseminating company.⁵⁵ Lastly, manufacturers must include a bibliography of similar research.⁵⁶ While FDAMA opened the door slightly to the dissemination of some off-label information, it placed significant limitations on the exchange of scientific information between pharmaceutical companies and healthcare professionals.

III. PROCEDURAL HISTORY OF THE WLF CASES AND THE NEW FRAMEWORK ESTABLISHED

In 1993, the WLF, a public interest law and policy center, filed a citizen's petition with the FDA challenging the agency's restrictions on distribution of off-label information by manufacturers on constitutional grounds.⁵⁷ The FDA did not grant the petition, and the WLF filed a lawsuit in 1994 challenging the FDA's restrictions based on the First Amendment.⁵⁸ The FDA unsuccessfully challenged the action on procedural grounds: first ripeness and then standing.⁵⁹

On July 30, 1998, the U.S. District Court for the District of Columbia found the FDA's restrictions on the dissemination of off-label information to be in conflict with the First Amendment and entered an injunction against FDA regulations restricting manufacturer dissemination of the kinds of off-label articles described in the order.⁶⁰ The court determined that dissemination of information by pharmaceutical companies constituted commercial speech, not pure speech.⁶¹ In determining whether the FDA's restrictions on this commercial speech were unconstitutional, the court applied the four-prong test set forth by the Supreme Court in *Central Hudson Gas & Electric Corp. v. Public Service Commission of New York*.⁶² Under this test, the government can restrict commercial speech if: (a) the speech is unlawful or inherently misleading; (b) the government's interest in the speech is substantial; (c) the restrictions on speech directly advance the government's interest; and (d) the means employed

55. *See id.*

56. *See id.* § 360aaa(b)(6)(B).

57. *See* Washington Legal Found. v. Kessler, 880 F. Supp. 26, 30 (D.D.C. 1995). At issue was an FDA policy that prohibited the dissemination of off-label information by a manufacturer except in very narrow circumstances. *See id.* at 27-28.

58. *See id.* at 30.

59. *See id.* at 31-36.

60. *See* Washington Legal Found. v. Friedman, 13 F. Supp. 2d 51, 74 (D.D.C. 1998), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000). By the time this case was heard the FDA's policies on dissemination of off-label information had been published as Guidance Documents. *See supra* note 39 and accompanying text.

61. *See* Friedman, 13 F. Supp. 2d at 65. How speech is classified is very important to the court's analysis. "[C]ommercial speech, . . . is subject to a more relaxed inquiry than core First Amendment speech." *Id.* at 59. The primary purpose of this doctrine is the protection of "consumers from misleading, deceptive or aggressive sales practices." *Id.* at 65 (quoting 44 Liquormart, Inc. v. Rhode Island, 517 U.S. 484, 501 (1996)).

62. *See id.* at 65-74.

fit the end sought.⁶³

In applying the first prong of the *Central Hudson* test, the court found that this type of speech-dissemination of off-label information is neither unlawful nor inherently misleading.⁶⁴ Under the second prong, the court found that Congress' mandate that the FDA must prove all drugs safe and effective established the FDA's interest in limiting off-label information as substantial.⁶⁵ Under the third prong, the court determined incentives for manufacturers to do clinical testing necessary for FDA approval directly advanced the government's interests.⁶⁶ Finally, under the fourth prong of the test, the court held that the means employed by the FDA were more extensive than necessary and that other less restrictive alternatives could be employed to advance the FDA's interests.⁶⁷ However, this decision did not resolve the issue because Congress contemporaneously enacted the FDAMA. Section 401 of this new act addressed manufacturer dissemination of off-label information and established a new regulatory framework.⁶⁸ Therefore, the parties returned to court seeking clarification of WLF I's decision as applied to the FDAMA. In WLF II, the same court held that the injunction also applied to Section 401 of the recently enacted FDAMA.⁶⁹

The decision in WLF I established the framework under which the dissemination of off-label information could occur by defining what the FDA could and could not restrict. In WLF I, the court enjoined the FDA from prohibiting, restricting, sanctioning, or in any way limiting pharmaceutical or device manufacturers from doing the following:

- a) from disseminating or redistributing to physicians or other medical professionals any article concerning prescription drugs or medical devices previously published in a bona fide peer-reviewed professional journal, regardless of whether such article includes a significant or exclusive focus on uses of drugs or medical devices other than those approved by FDA and regardless of whether such

63. See *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of New York*, 447 U.S. 557, 564-66 (1980).

64. See *Friedman*, 13 F. Supp. 2d at 69.

65. See *id.* at 71.

66. See *id.* at 72.

67. See *id.* at 73-74. The court proposed less restrictive alternatives, including "full, complete, and unambiguous disclosure" by the pharmaceutical company. *Id.* at 73. "Full disclosure not only addresses all of the concerns advanced by the FDA, but addresses them more effectively." *Id.* The court also suggested that pharmaceutical companies still have incentives to seek approval from the FDA for new uses, including potential protections under some tort law principles, and are still prohibited from "producing and distributing any internally-produced marketing materials to physicians concerning off-label uses." *Id.*

68. See *supra* note 47 and accompanying text.

69. See *Washington Legal Found. v. Henney*, 56 F. Supp. 2d 81 (D.D.C. 1999), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000).

article reports the original study on which FDA approval of the drug or device in question was based;

- b) from disseminating or redistributing to physicians or other medical professionals any reference textbook (including any medical textbook or compendium) or any portion thereof published by a bona fide independent publisher and otherwise generally available for sale in bookstores or other distribution channels where similar books are normally available, regardless of whether such reference textbook or portion thereof includes a significant or exclusive focus on uses of drugs or medical devices other than those approved by FDA; or
- c) from suggesting content or speakers to an independent program provider in connection with a continuing medical education seminar program or other symposium, regardless of whether uses of drugs and medical devices other than those approved by FDA are to be discussed.⁷⁰

On the other hand, the court recognized that the FDA could require a pharmaceutical manufacturer to disclose its financial interest in the study discussed and to disclose that the use being discussed in the study does not have FDA approval.⁷¹ Finally, the court held that the FDA would continue to have authority to regulate articles or texts that were false or misleading.⁷² The decisions in WLF I and WLF II represent significant departure from the previous regulatory regime.

In response to these decisions, the FDA appealed WLF II, “contending that the district court erred in concluding the FDAMA . . . [is] unconstitutional.”⁷³ The U.S. Court of Appeals for the District of Columbia Circuit heard the case on January 10, 2000 and issued its opinion a month later on February 11, 2000.⁷⁴ The Court’s decision has been called unclear, and both parties claimed victory after hearing the ruling.⁷⁵

Interestingly, the court did not reach the constitutional issue.⁷⁶ Instead, the court dismissed the FDA’s appeal and vacated the district court’s decisions and

70. *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 74-75 (D.D.C. 1998), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000). The court also provided definitions for “bona fide peer-reviewed journal,” “bona fide independent publisher,” and “independent program provider” to help decrease any potential confusion. *Id.* at 75.

71. *See id.*

72. *See id.*

73. *Washington Legal Found. v. Henney*, 202 F.3d 331, 335 (D.C. Cir. 2000).

74. *See id.* at 331.

75. *See discussion supra* note 5.

76. *See Henney*, 202 F.3d at 336. “The stage therefore appeared set for us to consider a difficult constitutional question of considerable practical importance. However, as a result of the government’s clarification at oral argument, the dispute between the parties has disappeared before our eyes.” *Id.* at 335.

injunctions, “insofar as they declare the FDAMA . . . unconstitutional.”⁷⁷ The court further explained in a footnote, “[a]s we have made clear, we do not reach the merits of the district court’s First Amendment holdings and part of its injunction still stands.”⁷⁸ The court’s decision appears to be based on the FDA’s assertions that the FDAMA did not authorize the FDA to restrict speech. Instead, the FDA asserted the FDAMA “established nothing more than a ‘safe harbor’ ensuring that certain forms of conduct would not be used against manufacturers in misbranding and ‘intended use’ enforcement actions based on pre-existing legislative authority.”⁷⁹ Once WLF heard the FDA’s position, their attorney stated in oral argument that WLF no longer had a constitutional objection to the FDAMA.⁸⁰

However, the FDA maintained that it could use “[dissemination of off-label information] as evidence in a misbranding or ‘intended use’ enforcement action.”⁸¹ The court left open the possibility that a manufacturer “may still argue that the FDA’s use of a manufacturer’s promotion of off-label uses as evidence in a particular enforcement action violates the First Amendment.”⁸² Again, the decision is unclear at best. Once the FDA clarified its position on the FDAMA, the court of appeals was of the opinion that the constitutional issues were removed.⁸³ Left open is whether the FDA’s ability to utilize other provisions of the FDCA to limit the dissemination of off-label information and bring enforcement actions against manufacturers could successfully be challenged as unconstitutional. While an extremely important issue, the constitutional questions presented by the WLF cases are not the focus of this Note. Instead this Note addresses the ability of the combination of the previously established framework in WLF I plus product liability law, unfair competition laws, and the pharmaceutical marketplace to protect society from the purported harms of this

77. *Id.* at 337.

78. *Id.* at 337 n.7. However, on November 30, 2000, the District Court for the District of Columbia denied a motion by WLF to confirm and enforce whatever portion of the injunction remained intact following the court of appeals’ decision. The motion made by WLF was prompted by the FDA’s March 16, 2000 Notice published in the Federal Register that outlined the FDA’s opinion of their scope of authority after the court of appeals’ decision. Although the court of appeals’ decision appeared to potentially leave the injunction intact in so far as it was not based on the federal constitution, the district court found that the injunction was based entirely on the federal constitution, and as a result no portion of the injunction remains in effect. Judge Lamberth was notably frustrated in how the court of appeals avoided the constitutional question, and his opinion suggests that if the FDA uses dissemination of off-label information as part of an enforcement action against a pharmaceutical manufacturer, the manufacturer will have a legitimate constitutional argument, at least if they wind up back in his court. See *Washington Legal Found. v. Henney*, No. 94-1306 (D.D.C. Nov. 30, 2000).

79. *Henney*, 202 F.3d at 335.

80. See *id.* at 336.

81. *Id.*

82. *Id.* at 336 n.6.

83. See *supra* note 76.

practice while allowing dissemination by manufacturers of truthful information on the off-label uses of pharmaceuticals.

IV. OTHER IMPORTANT PROTECTIONS RELATING TO THE DISSEMINATION OF OFF-LABEL INFORMATION

While some contend that the best way to protect society from indiscriminate drug use is for the FDA to tightly control the dissemination of off-label information and that the holdings in the WLF I and II jeopardize patient safety, other protective mechanisms are already in place. The three most important protections for society are potential product liability claims, potential claims by competitors under the Lanham Act, and the pressures associated with the pharmaceutical market.

A. Product Liability

Pharmaceutical companies will need to balance the benefit of disseminating off-label information with the increased risk of product liability claims. Product liability claims can have a significant economic impact, costing defendants millions of dollars.⁸⁴ In a sense, tight control over off-label information by the FDA actually prevented companies from injuring themselves.⁸⁵ Although ultimately settled out of court, American Home Products argued that they should not be liable for alleged harms resulting from the off-label use of the fen-phen combination because they did not disseminate information on this use.⁸⁶ Product liability claims are a mechanism for consumers to seek compensation for product-related injuries (including those caused by pharmaceuticals), and courts appear undecided on how to address uses of medications not approved by the FDA.

Cases involving design or manufacturing defects in pharmaceuticals are rare.⁸⁷ The reasons for this are varied, but generally it is because Good

84. In 1984, A.H. Robins lost fourteen product liability cases with average awards being \$4.1 million. In 1986, Merrell Dow lost eleven cases with average awards of \$7.1 million. See W. Kip Viscusi et al., *A Statistical Profile of Pharmaceutical Industry Liability, 1976-1989*, 24 SETON HALL L. REV. 1418, 1428 (1994). More recently, American Home Products settled a wrongful-death lawsuit relating to use of one of its former diet drugs for an amount believed to be about \$10 million. See Robert Langreth & Richard B. Schmitt, *American Home Settles Diet-Drug Case, Woman's Estate to Get About \$10 Million*, WALL ST. J., Jan. 28, 2000, at B9. In a similar lawsuit, a jury ordered American Home Products to pay more than \$23 million, sending the company's stock down twelve percent. See Robert Langreth, *American Home Is Ordered to Pay \$23.36 Million in Diet-Drug Suit*, WALL ST. J., Aug. 9, 1999, at A4.

85. See Amy Barrett, *Take Only As Directed (Wink)*, BUS. WK., Aug. 16, 1999, at 44. "The FDA prevented you from doing a lot of injury to yourself." *Id.* (quoting William W. Vodra, an attorney who represented American Home Products).

86. See *id.* American Home Products, a large pharmaceutical company, manufactured fenfluramine, the "fen" portion of fen-phen, a popular combination used for weight loss.

87. See Michael D. Green, *Safety as an Element of Pharmaceutical Quality: The Respective*

Manufacturing Practices (GMPs) are followed closely by the industry and monitored by the FDA.⁸⁸ Additionally, it is difficult for plaintiffs to demonstrate that an alternative design for a pharmaceutical was technically feasible.⁸⁹ Also, in order to prevail in a design defect case, the plaintiff must be able to show that the foreseeable risks of the pharmaceutical outweigh its foreseeable therapeutic benefits.⁹⁰ Courts have been reluctant to find that a drug's overall risks outweigh its benefits.⁹¹ As a result, most pharmaceutical product liability cases deal with failure to warn.⁹²

According to the Restatement (Third) of Torts:

A prescription drug or medical device is not reasonably safe due to inadequate instructions or warnings if reasonable instructions or warnings regarding foreseeable risks of harm are not provided to:

- (1) prescribing and other health-care providers who are in a position to reduce risks of harm in accordance with the instructions or warnings; or
- (2) the patient when the manufacturer knows or has reason to know that health-care providers will not be in a position to reduce the risks of harm in accordance with the instructions or warnings.⁹³

Historically, courts have held that a manufacturer typically does not need to warn patients directly.⁹⁴ Instead the manufacturer must only warn the physician

Roles of Regulation and Tort Law, 42 ST. LOUIS U. L.J. 163, 168 (1998). A product has "a manufacturing defect when the product departs from its intended design even though all possible care was exercised in the preparation and marketing of the product." RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2(a) (1997). A product has a design defect when "the foreseeable risks of harm posed by the product could have been reduced or avoided by the adoption of a reasonable alternative design by the seller or other distributor." RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2(b) (1997).

88. See Green, *supra* note 87, at 168.

GMP's mean the requirements found in the legislations, regulations, and administrative provisions for methods to be used in, and the facilities or controls to be used for, the manufacturing, processing, packing, and/or holding of a drug to assure that such drug meets the requirements as to safety, and has the identity and strength, and meets the quality and purity characteristics that it purports or is represented to possess.

21 C.F.R. § 26.1(c)(1) (2000).

89. See Green, *supra* note 87, at 168.

90. See RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 8 (1997).

91. See Green, *supra* note 87, at 169.

92. See *id.*

93. RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 6(d) (1997).

94. See *Sottlemire v. Cawood*, 213 F. Supp. 897 (D.D.C. 1963); *cf. Perez v. Wyeth Lab., Inc.*, 734 A.2d 1245 (N.J. 1999) (holding that with regard to an implanted birth control device the manufacturer had a duty to warn patients directly). Courts have held that "[o]ral contraceptives . . . bear peculiar characteristics which warrant the imposition of a common law duty on the manufacturer to warn users directly of associated risks." *MacDonald v. Ortho Pharm. Corp.*, 475

who prescribes the medication. This is called the “learned intermediary” doctrine.⁹⁵ Because the physician is in the best position to determine whether the benefits of the drug outweigh its risks for the particular patient, the doctrine exempts manufacturers from liability if it provides a physician with all information available to allow the physician to make an informed medical judgment.⁹⁶ Currently, all product liability cases are decided under state standards, because no federal product liability law exists.⁹⁷

One reason manufacturers resist disseminating off-label information is that FDA approval provides some protection. In some ways, the FDA’s prohibition on dissemination of off-label information has actually protected pharmaceutical companies from themselves.⁹⁸ At least four states (Arizona, Ohio, Oregon, and Utah) have statutes that bar punitive damages in cases where the manufacturer complied with FDA regulations in bringing a product to market, including packaging and labeling provisions.⁹⁹ Additionally, FDA approval is at least one factor considered by other jurisdictions that do not have a statutory defense.¹⁰⁰

There is also a growing movement that FDA approval should provide even more protection for pharmaceutical manufacturers. In fact, several commentators have suggested that FDA approval should be an absolute bar to product liability actions, dubbed the “FDA Defense,” and advance several rationales. First, the FDA makes a risk/benefit decision when it approves new drugs and new indications.¹⁰¹ Second, the FDA is in a better position than judges or juries to make these determinations.¹⁰² Third, the FDA regulates the labeling and therefore controls “warnings.”¹⁰³ Fourth, the FDA is effective in enforcing its regulations.¹⁰⁴ Finally, federal preemption of state law would lead to more

N.E.2d 65, 69 (Mass. 1985).

95. See *Johnson v. Am. Cyanamid Co.*, 718 P.2d 1318, 1324 (Kan. 1986), *aff’d*, 758 P.2d 206 (Kan. 1988).

96. See *id.*; Jeffrey N. Gibbs & Bruce F. Mackler, *Food and Drug Administration Regulation and Products Liability: Strong Sword, Weak Shield*, 22 TORT & INS. L.J. 194, 198-99 (1987).

97. See Gibbs & Mackler, *supra* note 96, at 197.

98. See discussion *supra* note 85.

99. See ARIZ. REV. STAT. § 12-701 (1992); OHIO REV. CODE ANN. § 2307.801(C)(1)(a) (2000); OR. REV. STAT. § 30.927(1) (1999); UTAH CODE ANN. § 78-18-2 (1999); see also Annette L. Marthaler, *The FDA Defense: A Prescription for Easing the Pain of Punitive Damage Awards in Medical Products Liability Cases*, 19 HAMLIN L. REV. 451, 461 (1996) (reviewing actions states have taken to implement an FDA Defense).

100. See Gibbs & Mackler, *supra* note 96, at 222; Jeffrey D. Winchester, *Section 8(C) of the Proposed Restatement (Third) of Torts: Is it Really What the Doctor Ordered?*, 82 CORNELL L. REV. 644, 656 (1997).

101. See Michael D. Green, *Statutory Compliance and Tort Liability: Examining the Strongest Case*, 30 U. MICH. J.L. REFORM 461, 474 (1997).

102. See *id.* at 477; David S. Torborg, *Design Defect Liability and Prescription Drugs: Who’s in Charge?*, 59 OHIO ST. L.J. 633, 650 (1998).

103. See Green, *supra* note 101, at 475-76.

104. See Marthaler, *supra* note 99, at 483.

consistent outcomes.¹⁰⁵ If the proponents of the FDA defense prevail, pharmaceutical manufacturers will have significant incentives to seek FDA approval for new indications and changes in dosing and administration. As discussed below, even without such reform, the current environment that recognizes FDA-approval as at least a partial defense in a product liability lawsuit guides some pharmaceutical companies not to share information about off-label uses in certain jurisdictions.

Courts have utilized various approaches in addressing product liability claims stemming from off-label uses. One court held that a manufacturer is never liable for failure to warn of risks associated with off-label use.¹⁰⁶ Other courts have found no distinction between obligations associated with on- or off-label uses,¹⁰⁷ and others have looked to the acceptance of the use by the general medical community.¹⁰⁸ Another court based its decision on whether the manufacturer had benefitted from the use.¹⁰⁹ Finally, some courts have imposed liability when the

105. See Torborg, *supra* note 102, at 657.

106. See *Robak v. Abbott Lab.*, 797 F. Supp. 475 (D. Md. 1992). A physician prescribed an antibiotic for a use that was not approved by the FDA and was not in the antibiotic's FDA-approved labeling. See *id.* Additionally, the plaintiff presented evidence that the manufacturer had made claims that the antibiotic was effective in conditions beyond the approved labeling. See *id.* at 476. However, the court stated, "[i]t stands to reason that when a physician, as a learned intermediary, has been provided with the indications for which a drug is effective, but prescribes it for a non-indicated use, the manufacturer should not be exposed to tort liability for any defect in labeling." *Id.* at 476.

107. See *Hahn v. Richter*, 628 A.2d 860 (Pa. Super. Ct. 1993), *aff'd*, 673 A.2d 888 (Pa. 1996). A physician administered an injectable steroid in the spine, which was a route of administration that was not approved by the FDA. See *id.* The plaintiff alleged that the manufacturer knew or should have known of risks associated with this route of administration and also knew or should have known that physicians were using the product in this way. See *id.* at 863. The court did not distinguish between on- and off-label uses in its analysis. See *id.* at 863-68.

108. See *Upjohn Co. v. MacMurdo*, 562 So. 2d 680 (Fla. 1990). The plaintiff suffered injuries from the off-label use of a product for contraception, which was generally accepted in the medical community. See *id.* at 683. In the FDA-approved labeling for the product, the manufacturer stated that use of the product for contraception was investigational and not approved by the FDA; however, the court rejected the argument that the manufacturer had met its burden by warning that this use was not approved by the FDA. See *id.* at 682-83. This apparently suggests that if the use was generally accepted in the medical community, then the manufacturer had an additional duty to warn of adverse events associated with that use. See *id.* at 683.

109. See *Miles Lab., Inc. v. Superior Court*, 184 Cal. Rptr. 98 (Cal. Ct. App. 1982). A plaintiff suffered from injuries resulting from the off-label use of a product to prevent miscarriages and sued several manufacturers of the product. See *id.* at 99. One of the manufacturers alleged that its product had been developed for its FDA-approved use only and that it did not participate in any activities associated with getting physicians to use the product for the unapproved use. See *id.* at 99-100. However, a portion of the manufacturer's sales of the product was the result of the off-label use. See *id.* at 103. The court held that if the manufacturer knew or should have known of the off-label use and also benefitted from the off-label use, then it had a duty to warn of the possible

off-label use was foreseeable.¹¹⁰ It is worth noting that all of the cases were decided when pharmaceutical manufacturers were prohibited from disseminating unsolicited information about off-label uses. One might predict that once manufacturers begin dissemination of off-label information under the rulings in WLF I and WLF II, the distinction between on- and off-label uses will begin to blur. These differences in state laws create challenges for pharmaceutical companies that promote and sell their products across many jurisdictions.

The plaintiffs in *In re Orthopedic Bone Screw Products Liability Litigation* recently advanced a separate but related cause of action: "fraud on the FDA."¹¹¹ In the case, the Third Circuit reversed a lower court ruling that a plaintiff could not bring a cause of action under the FDCA.¹¹² The case involved a device manufacturer and its consultant who first submitted to the FDA a request for approval for one use of its products that was denied.¹¹³ The company then sought approval for another use, which was granted.¹¹⁴

The plaintiffs alleged that the manufacturer made material misrepresentations to the FDA and sought approval for the later use only as a pretext to make the product available for the previously rejected use.¹¹⁵ The court held that "the plaintiffs' 'fraud on the FDA' theory of liability is not so at odds with traditional principles of tort law that [the manufacturer] is entitled to a dismissal of all claims against it at this stage."¹¹⁶ Notably, the company tried to pursue an indication for the unapproved use at issue and their data was rejected by the FDA. This, as well as other facts negative to the manufacturer, likely makes this case distinguishable. Nevertheless, this case suggests that manufacturers who go for the easiest indications and then disseminate off-label information on other uses of their products might be at risk for this new, albeit untested, cause of action.

adverse effects associated with the off-label use. *See id.*

110. *See Medics Pharm. Corp. v. Newman*, 378 S.E.2d 487 (Ga. Ct. App. 1989). The plaintiff suffered injuries from the off-label use of a product to prevent miscarriage. *See id.* at 488. The court held that the manufacturer could be liable if the off-label use of the product to prevent miscarriages was foreseeable. *See id.* at 489; *see also* *Richards v. Upjohn Co.*, 625 P.2d 1192 (N.M. Ct. App. 1980). The plaintiff suffered from the off-label use of an antibiotic to irrigate a wound post-operatively. *See id.* at 1194. The use had previously been in the product's FDA-approved labeling; however, the manufacturer withdrew this use and no longer recommended the product for this use. *See id.* The court held that the manufacturer had a duty to warn of adverse events associated with the use of its product to irrigate wounds after surgery, if that use was foreseeable. *See id.* at 1195-97.

111. 159 F.3d 817, 818 (3d. Cir. 1998).

112. *See id.* at 819.

113. *See id.* at 820.

114. This case dealt with the approval of medical devices, which are approved under a different regulatory framework from drugs, but the process is similar enough that a similar set of facts associated with a drug manufacturer could be considered analogous.

115. *See Orthopedic Bone Screw Prods.*, 159 F.3d at 820.

116. *Id.* at 829.

B. Lanham Act

Pharmaceutical companies will also need to consider potential attacks from competitors under the Lanham Act before disseminating off-label information. The Lanham Act provides a private cause of action for unfair competition resulting from false advertising, including false scientific establishment claims.¹¹⁷

The Lanham Act was passed in 1946, but was not extended to address false advertising about a competitor's product until 1954 when the Third Circuit decided *L'Aiglon Apparel, Inc. v. Lana Lobell, Inc.*¹¹⁸ In the case, L'Aiglon Apparel alleged that the defendant had wrongfully used a picture of the plaintiff's dress in a national advertising campaign.¹¹⁹ The plaintiff did not allege that the picture was used to mislead consumers into thinking that the dress being sold was manufactured by the plaintiff—a so-called "palming off" claim.¹²⁰ Rather, the plaintiff alleged that the defendant was misleading consumers by insinuating that they could receive a similar dress for less money.¹²¹ However, even after *L'Aiglon Apparel*, other jurisdictions continued to limit the Act by disallowing similar claims; only misrepresentations made about one's own product were covered.¹²² Thus, the Act effectively protected consumers more than competitors. Congress finally spoke in 1988, expressly rejecting precedent contrary to *L'Aiglon Apparel* and indicating that the Lanham Act was intended to protect both consumers and competitors. Misrepresentations about a competitor's product, as well as the manufacturer's own product, are now actionable under the Act.¹²³

Currently, a Lanham Act false advertisement claim requires five essential elements. First, the plaintiff must show that the defendant made "false or misleading statements."¹²⁴ This includes false statements about scientific data. Second, the plaintiff must show "there is actual deception or at least a tendency

117. See 15 U.S.C.A. § 1125(a) (1999). In early Lanham Act cases, courts limited the Act to "palming-off" claims. These were misrepresentations made by manufacturers that their product originated from another source. See *Chamberlain v. Columbia Pictures Corp.*, 186 F.2d 923, 925 (9th Cir. 1951); Charles J. Walsh & Marc S. Klein, *From Dog Food to Prescription Drug Advertising: Litigating False Scientific Establishment Claims Under the Lanham Act*, 22 SETON HALL L. REV. 389, 409 (1992). Establishment claims entered Lanham Act jurisprudence in 1986 in *Thompson Medical Co. v. Ciba-Geigy Corp.*, 643 F. Supp. 1190 (S.D.N.Y. 1986). See Walsh & Klein, *supra*, at 419.

118. 214 F.2d 649 (3d Cir. 1954).

119. See *id.* at 650.

120. See discussion *supra* note 116.

121. See *L'Aiglon Apparel*, 214 F.2d at 650.

122. See *Bernard Food Indus., Inc. v. Dietene Co.*, 415 F.2d 1279 (7th Cir. 1969).

123. See Walsh & Klein, *supra* note 116, at 409-11.

124. *United States Healthcare, Inc. v. Blue Cross of Greater Philadelphia*, 898 F.2d 914, 922 (3d Cir. 1990) (quoting *Max Daetwyler Corp. v. Input Graphics, Inc.*, 545 F. Supp. 165, 171 (E.D. Pa. 1982)).

to deceive a substantial portion of the intended audience.”¹²⁵ Third, the plaintiff must demonstrate that “the deception is material in that it is likely to influence purchasing decisions.”¹²⁶ Fourth, for jurisdictional purposes, the goods being advertised must travel in interstate commerce.¹²⁷ Lastly, the plaintiff must demonstrate the “likelihood of injury to the plaintiff in terms of declining sales, loss of good will, etc.”¹²⁸ Injunctive relief is the usual remedy granted, but in some cases corrective advertising is granted.¹²⁹

Many of the Lanham Act cases associated with pharmaceutical products involve establishment claims. An establishment claim represents that scientific data or other information exists to support the truth of the statement.¹³⁰ Common fact patterns in Lanham Act cases include the following: (a) no “real” science, (b) distortion of science, (c) old science that is no longer relevant, (d) unreliable science, and (e) good science, but the data does not support the statement.¹³¹ Many courts have adopted FDA standards in evaluating scientific data.¹³²

A recent Lanham Act decision involving pharmaceutical products is *Zeneca Inc. v. Eli Lilly and Co.*¹³³ In this case, the plaintiffs alleged that Lilly was making false promotional claims about one of its products, raloxifene hydrochloride (Evista®).¹³⁴ At that time, Evista® had been approved by the FDA for the prevention of osteoporosis in postmenopausal women.¹³⁵ The plaintiffs’ products were FDA-approved for the treatment of advanced breast cancer.¹³⁶ The plaintiffs accused Lilly of claiming that Evista® (1) had been proven to reduce the risk of breast cancer, (2) was comparable or superior to tamoxifen citrate for the prevention of breast cancer and (3) had been approved by the FDA for prevention of breast cancer.¹³⁷ Lilly argued that it never made the latter two claims and that the first claim was not false, based on the results of a clinical trial known as the MORE study, the results of which were published in the *Journal*

125. *Id.*

126. *Id.*

127. *See id.*

128. *Id.* at 922-23.

129. *See* Walsh & Klein, *supra* note 116, at 416-18.

130. *See* William I. Rothbard, *Challenging False Advertising by Competitors*, 775 PLI/COMM. 23, 29 (1997).

131. *See* Walsh & Klein, *supra* note 116, at 423-28.

132. *See id.* at 429. The FDA uses the substantial evidence test for safety and efficacy of a drug. This includes data from well-controlled clinical investigations, conducted by qualified experts with the training and experience needed to assess the safety and efficacy of the drug. *See* 21 C.F.R. § 202.1(e)(4)(ii)(b) (2000). The FDA will also allow claims “[f]or which there exists substantial clinical experience.” 21 C.F.R. § 202.1(e)(4)(ii)(c).

133. No. 99-Civ.-1452(JGK), 1999 WL 509471 (S.D.N.Y. July 19, 1999).

134. *See id.* at *1.

135. *See id.*

136. *See id.*

137. *See id.*

of the American Medical Association (*JAMA*).¹³⁸ The court disagreed, holding that Lilly had made the first two claims and granting plaintiffs injunctive relief.¹³⁹

A key factor in the decision was the MORE study.¹⁴⁰ Certain results of the MORE study were published in the June 16, 1999 issue of *JAMA*. The authors concluded that "a median of [forty] months of treatment with raloxifene decreases the risk of newly diagnosed breast cancer in post-menopausal women who have osteoporosis and who have no prior history of breast cancer."¹⁴¹ While the court found the results of the study promising, it did not think Lilly demonstrated that Evista® reduced the risk of breast cancer.¹⁴² In making its decision, the court relied heavily on correspondence between the FDA and Lilly that suggested the MORE study could not, by itself, support an indication for the prevention of breast cancer.¹⁴³ However, the FDA rarely approves new products or new indications based solely on the results of one study. Further, the FDA allowed Lilly to add information about the results of the MORE study to the Evista® package insert, with the caveat that the following statement also be added: "the effectiveness of raloxifene in reducing the risk of breast cancer has not yet been established."¹⁴⁴

This decision produces uncertainty for pharmaceutical manufacturers wishing to disseminate off-label information without fear of a Lanham Act claim. Importantly, the court in this case found actual promotion, as opposed to dissemination, which is not protected by the WLF cases. This decision would seem to suggest that manufacturers have to be very careful that dissemination of off-label information does not turn into promotion. However, the line between promotion and dissemination can be blurry, and courts and the FDA may interpret the terms differently. This decision is disconcerting to proponents of free dissemination of off-label information because it implies that without FDA approval of information a manufacturer may be subjecting itself to the risk of a Lanham Act claim.

138. See *id.* at *26.

139. See *id.* at *43.

140. See Steven R. Cummings et al., *The Effect of Raloxifene on Risk of Breast Cancer in Postmenopausal Women*, 281 *JAMA* 2189 (1999). MORE is an acronym for Multiple Outcomes of Raloxifene Evaluation and was Lilly's registration clinical trial for the indication of treatment of osteoporosis in postmenopausal women. See *id.* at 2189. The MORE trial studied the effects of raloxifene on the risk of breast cancer as a secondary endpoint. See *id.* at 2190. The osteoporosis results were published in the August 18, 1999 issue of *JAMA*. See Bruce Ettinger et al., *Reduction of Vertebral Fracture Risk in Postmenopausal Women with Osteoporosis Treated with Raloxifene*, 282 *JAMA* 637 (1999).

141. Cummings et al., *supra* note 140, at 2196.

142. See *Zeneca Inc. v. Eli Lilly and Co.*, No. 99-Civ.-1452(JGK), 1999 WL 509471, at *43 (S.D.N.Y. July 19, 1999).

143. See *id.* at *18-22.

144. *Id.* at *27.

C. The Pharmaceutical Marketplace

Perhaps the strongest incentive for pharmaceutical manufacturers to think twice before providing off-label information about their product is the pharmaceutical marketplace itself.¹⁴⁵ Empirical data suggest that detailing, the interaction between the prescriber and a sales representative, has a direct effect on sales.¹⁴⁶ Additionally, an increasing number of sales representatives are vying for a physician's limited time,¹⁴⁷ with an increasing number of competitive products in the marketplace.¹⁴⁸ Intuitively, this leads to less time available for sales representatives to convince physicians to prescribe their products.

These time restrictions increase the need for sales representatives to share credible information with physicians. If a physician does not feel that the sales representative is sharing credible information, then he or she may refuse to see the representative, thus severing one of the pharmaceutical company's primary means of impacting market share. Consequently, a manufacturer will have incentives to ensure that their sales representatives do not promote from or overstate the significance of the scientific off-label information that is being shared. The physician can also choose to report false claims to the regulatory authorities if the representative is inappropriately characterizing the data. Additionally, because reputation and public perception play such a key role in the economic success of pharmaceutical companies, negative publicity associated with sharing false and/or misleading information will likely have an adverse effect on an individual company's financial success.¹⁴⁹

V. PROTECTIONS DO EXIST IF UNCERTAINTIES ARE RESOLVED

The framework established in WLF I coupled with product liability law, the Lanham Act, and the pharmaceutical marketplace could provide adequate protection for society, while at the same time allowing the important dissemination of off-label information about pharmaceutical products. However, manufacturers may not take full advantage of the WLF framework until the uncertainties that exist in current product liability law, the Lanham Act and the court of appeals' decision in *Washington Legal Foundation v. Henney* are resolved.

A. Product Liability

Two key uncertainties remain under current product liability law, primarily stemming from inconsistent treatment of the topic by the various jurisdictions.

145. See Winchester, *supra* note 100, at 645.

146. See John A. Rizzo, *Advertising and Competition in the Ethical Pharmaceutical Industry: The Case of Antihypertensive Drugs*, 42 J.L. & ECON. 89, 107 (1999).

147. See Larry Gabe & Michele Goldberg, *Employment Outlook '99: Still an Employee's Market*, PHARM. EXECUTIVE, Apr. 1, 1999, at 59, 1999 WL 11913794.

148. See Rizzo, *supra* note 146, at 107.

149. See Winchester, *supra* note 100, at 645.

The first is the distinction that some courts make between claims involving on-label and off-label use and the related status of an "FDA Defense."¹⁵⁰ The second is the ruling in *Orthopedic Bone Screw Products* that creates a potential cause of action for "fraud on the FDA," as discussed above.¹⁵¹

Congress could best address these inconsistencies by enacting a federal statute that includes some form of the FDA Defense.¹⁵² In 1995, a product liability bill was passed by the House of Representatives that contained an FDA Defense provision.¹⁵³ In the bill, punitive damages would not be awarded against a manufacturer if the product involved was "subject to premarket approval by the Food and Drug Administration . . . and such drug was approved by the Food and Drug Administration."¹⁵⁴ Punitive damages would also be barred if "the drug is generally recognized as safe and effective pursuant to conditions established by the Food and Drug Administration and applicable regulations, including packaging and labeling regulations."¹⁵⁵ Unfortunately, the House bill was not enacted into law, but the provisions contained therein represent a viable starting point. This defense would give pharmaceutical companies a significant incentive to conduct the additional studies needed to seek FDA approval for additional uses of their drugs, alleviating one of the FDA's main concerns about the WLF I and II decisions. Such a law would additionally create more certainty for manufacturers because it would negate the current, confusing distinctions across jurisdictions. In this new law, Congress could also outline how the courts should address the distinction between product liability cases involving on-label and off-label uses.

Utilization of the framework established in the Restatement (Third) of Torts dealing with failure to warn might be appropriate. Pharmaceutical companies should be required to provide physicians with enough information about the known benefits and risks of their products for the physician to make an informed decision. One proposal would be to create a duty to warn physicians of known potential adverse effects associated with off-label use for manufacturers that choose to disseminate off-label information related to that use. While it is not reasonable to hold a manufacturer responsible merely because its product is being prescribed for off-label use, it is reasonable to hold a manufacturer liable for not warning of known adverse effects associated with uses for which it actively disseminates information. The Restatement approach would both allow companies to utilize the WLF framework and could help alleviate concerns that these companies will not provide information on both the risks and benefits of the use of their products in unapproved indications.

150. See *supra* note 101-10 and accompanying text.

151. See *supra* notes 111-16 and accompanying text.

152. The FDA Defense was proposed in two separate bills in 1995, each containing provisions for FDA approval limiting the liability of pharmaceutical manufacturers in product liability cases. See Marthaler, *supra* note 99, at 472.

153. See H.R. 956, 104th Cong., § 201(f) (1995).

154. H.R. 956, 104th Cong., § 201(f)(1)(A)(i) (1995).

155. H.R. 956, 104th Cong., § 201(f)(1)(A)(ii) (1995).

Even if Congress took the above actions, however, the *Orthopedic Bone Screw Products* ruling might still be of concern. While likely distinguishable, this case seems to stand for the proposition that a cause of action exists when companies pursue regulatory approval for one use of their products and then disseminate information on another unapproved use. Admittedly, this case involved devices instead of pharmaceuticals, but the reasoning by the court could easily apply to both. Moreover, the company tried to pursue an indication for the unapproved use at issue and their data were rejected by the FDA. Typically, manufacturers will be disseminating cutting-edge data that have not yet been reviewed by the FDA. Nevertheless, in order for companies to disseminate off-label information without fear of similar lawsuits, this holding would need to be overruled.

B. Lanham Act

The most recent pharmaceutical Lanham Act case, *Zeneca, Inc. v. Eli Lilly and Co.*,¹⁵⁶ presents another possible barrier to a less-restricted exchange of off-label information. The case suggests that even though data was published in a peer-reviewed journal, off-label information could still be considered false and misleading under the Lanham Act criteria. Importantly, the court in this case found promotion and not just dissemination, but the line between the two can be blurry. As a result, manufacturers must ensure that dissemination efforts do not rise to the level of promotion. Additionally, manufacturers' compliance with the WLF I framework may not preclude a Lanham Act claim.

Dissemination of scientific data published in a peer-reviewed journal should not be deemed false and misleading simply because the FDA does not consider it sufficient evidence to determine an indication for a use. The FDA only on very rare occasions will approve new products or new uses based on a single study. If this case implies that a manufacturer cannot disseminate scientific information unless it has the kind of "substantial evidence" required for FDA-approval of that use, then the rights granted under WLF I and II have little value to physicians, their patients or manufacturers. Clearly, clinical trial data can be presented out of context or misconstrued, but if a study is published in a peer-reviewed journal, the data in that article should not, by definition, be considered false. Courts should, of course, apply the Lanham Act when manufacturers misrepresent good science or try to utilize old science that is no longer relevant, but should not construe "false and misleading" as equivalent to not meeting the evidentiary standard utilized by the FDA.

C. Washington Legal Foundation Cases

The lack of clarity provided by the appellate court will lead to cautious utilization of WLF I framework by pharmaceutical manufacturers. Companies will have concerns about the FDA's response to manufacturers embracing the new framework and ignoring the guidelines established by the agency (and

156. No. 99-Civ.-1452 (JGK), 1999 WL 509471 (S.D.N.Y. July 19, 1999).

FDAMA). These concerns include fear of retaliation by the agency¹⁵⁶ and enforcement actions for misbranding.¹⁵⁷ Importantly, the FDA continues to view "off-label" dissemination as inconsistent with its goals of inducing manufacturers to submit new evidence of effectiveness for supplemental labeling.¹⁵⁸

A higher court reaching the merits of the First Amendment issue in the current case could best address the lack of clarity in this area. A court could also resolve the issue if the FDA brings an enforcement action against a pharmaceutical manufacturer and the company challenges the constitutionality of the FDA's action. The U.S. Court of Appeals in *Washington Legal Foundation v. Henney* did question whether the FDA could use evidence of off-label dissemination as grounds for an enforcement action without violating the First Amendment.¹⁵⁹ The previous opinions by the District Court for the District of Columbia suggest a pharmaceutical manufacturer could prevail with a First Amendment argument.¹⁶⁰ While both steps provide some clarity on the issue, manufacturers likely will be reluctant to go to battle with the FDA for the reasons discussed above.

Another possibility would be for Congress to amend the FDCA to comport with the framework established by WLF I. This would likely mean amending the provisions of the FDCA and FDAMA that are in conflict with a free exchange of scientific data between healthcare professionals and manufacturers. This approach would seem to be beneficial for both the FDA and manufacturers. It would prevent the FDA from retreating on the agency's long-held aversion toward off-label dissemination. Moreover, it would allow manufacturers to receive the benefits of off-label dissemination without fear of an enforcement action or retaliation by the agency.

CONCLUSION

WLF I and II have increased the ability of pharmaceutical manufacturers to disseminate off-label information about their products. To some this means that healthcare professionals will receive the latest, most innovative information available about the products they prescribe and be better equipped to treat suffering patients. To others this spells disaster and puts patients and the companies themselves at risk.

156. See Jeff Swiatek, *Off-label Ruling Opens Door for Lilly; Drugmaker's Sales Reps Can Offer Doctors Articles That Describe Other Uses for Products*, INDPLS. STAR, July 30, 1999, at C1.

157. See discussion *supra* note 46.

158. See discussion *supra* notes 27-35 and accompanying text.

159. A manufacturer "may still argue that the FDA's use of a manufacturer's promotion of off-label uses as evidence in a particular enforcement action violates the First Amendment." *Washington Legal Found. v. Henney*, 202 F.3d 331, 336 n.6 (D.C. Cir. 2000).

160. See *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000); *Washington Legal Found. v. Henney*, 56 F. Supp. 2d 81 (D.D.C. 1999), *appeal dismissed, vacated in part*, 202 F.3d 331 (D.C. Cir. 2000); *Washington Legal Found. v. Henney*, No. 94-1306 (D.D.C. Nov. 30, 2000).

The framework established in WLF I, coupled with product liability law, the Lanham Act, and the pressures of the pharmaceutical marketplace can allow pharmaceutical companies to disseminate off-label information, while still leaving tools available to ensure that the information being disseminated is not misleading. However, uncertainties still remain and need to be addressed. Product liability law relating to pharmaceuticals is inconsistent across the country, recent Lanham Act decisions appear to conflict with the principles of the WLF cases, and the remaining effect of the WLF cases remains uncertain.

Nevertheless, solutions do exist. Congress and the courts could take steps to resolve these issues and ensure that important information on off-label uses of life-saving pharmaceuticals is readily available to physicians and that adequate protections are in place to protect society from over-zealous marketing activities.

