



DIGITAL ACCESS TO SCHOLARSHIP AT HARVARD

FDA's Position on Off-Label Use and Promotion of Drugs and Devices and Recent Enforcement Efforts by the Department of Justice

The Harvard community has made this article openly available. [Please share](#) how this access benefits you. Your story matters.

| | |
|---------------------|--|
| Citation | Suzanne Foster, FDA's Position on Off-Label Use and Promotion of Drugs and Devices and Recent Enforcement Efforts by the Department of Justice (April 2009). |
| Accessed | February 19, 2015 9:21:24 AM EST |
| Citable Link | http://nrs.harvard.edu/urn-3:HUL.InstRepos:8789612 |
| Terms of Use | This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA |

(Article begins on next page)

FDA's Position on Off-Label Use and Promotion of Drugs and Devices and
Recent Enforcement Efforts by the Department of Justice

Suzanne Foster

Harvard School of Public Health, Class of 2009

April 5, 2009

Submitted in satisfaction of the course requirement

ABSTRACT

Off-label drug or medical device “use” is the practice of prescribing drugs or medical devices to patients for a purpose not included on the federally approved label. Off-label “marketing” is the practice of attempting to influence physicians to prescribe drugs or devices for off-label purposes. The Federal Food and Drug Administration (FDA) maintains regulatory authority over the proper labeling of drugs and medical devices. This paper summarizes the FDA’s position on off-label use, promotion, and marketing and provides a summary of recent enforcement actions by the U.S. Department of Justice regarding off-label marketing.

I. Introduction

On January 15, 2009, the United States Justice Department (DOJ) announced that Eli Lilly and Company had agreed to pay a criminal fine of \$515 million to resolve allegations that the company promoted one of its drugs for uses not approved by The United States Food and Drug Administration (FDA).¹ In addition to the \$515 million criminal fine, Eli Lilly agreed to forfeit \$100 million in assets and pay up to \$800 million to compensate states and the federal government for “false claims” paid by government payors who reimbursed for off-label uses that were allegedly the result of the physician

¹ U.S. Department of Justice, Eli Lilly and Company agrees to pay \$1.415 billion to resolve allegations of off-label promotion of Zyprexa. No. 09-038. January 15, 2009. Available at: <http://www.usdoj.gov/opa/pr/2009/January/09-civ-038.html>. Accessed March 30, 2009.

being improperly influenced to prescribe the drug.² In total, the company will pay \$1.415 billion.³

Two weeks later, on January 26, 2009, Pfizer agreed to a \$2.3 billion settlement for the off-label promotion of one of its drugs.⁴ This was not the first settlement for Pfizer for similar allegations; Pfizer (on behalf of Warner-Lambert) paid \$430 million in 2004 for the off-label promotion of Neurontin.⁵ And there appears to be more settlements in process between pharmaceutical and medical device companies and the government.⁶ For example, in February 2009, GlaxoSmithKline warned that its earnings in 2008 would be affected by a \$400 million legal charge related to the five year investigation into “marketing and promotional practices for several products for the period of 1997 through 2004.”⁷

At the same time that the DOJ is announcing these tremendous criminal fines, the FDA is offering a seemingly different approach to off-label marketing by relaxing its former view on off-label promotion by drug and device manufacturers. Interestingly, two months earlier in November 2008, another federal agency the Center for Medicare and Medicaid (CMS) announced that it was expanding Medicare coverage to include off-

² Id.

³ Id.

⁴ Edwards J. How Pfizer hid a 2.3 bill. Bextra settlement in plain sight. BNet. January 26, 2009. Available at: <http://industry.bnet.com/pharma/1000656/how-pfizer-his-s-23-bill-bextra-settlement-in-plain-sight/>. Accessed March 29, 2009.

⁵ Verdict /Settlement, U.S. ex rel. David Franklin v. Parke-Davis, No. 96-11651 PBS (D. Mass, May 13, 2004).

⁶ Feds Look to Extend Off-Label marketing Streak with J7J, February 20, 2009 accessed at: <http://blogs.wsj.com/health/2009/02/20/feds-llok-to-extend-off-label-marketing-streak-with-j&j.com>

⁷ Whalen J. Glaxo warns of charge, hints at pact. Wall Street Journal January 30, 2009:B3. Available at: <http://online.wsj.com/article/SB123327051846730799>. Accessed March 30, 2009.

label uses of chemotherapy drugs.⁸ So if off-label promotion is a serious crime, one that warrants billions of dollars in criminal fines, how does one interpret the actions of the FDA to expand permissible off-label promotion? And, although not discussed in depth in this paper, yet warrants thought, is how does one interpret the decision by CMS to pay for chemotherapy drugs for off-label use based on recommendations from sources that are influenced by the manufacturers of chemotherapy drugs?⁹ While these actions by the U.S. Justice Department, FDA, and CMS seem to be in conflict, an alternative argument is that while off-label use is appropriate and beneficial in some circumstances it is not safe and effective in others. And for those that can play by the rules off-label use remains available to them, but for the others seemingly motivated by ill intent the message is be prepared to pay.

II. The FDA's Evolving Position on Off-label

The FDA's mission is to promote and protect the public health.¹⁰ So when it comes to off-label use of drugs, the FDA must balance two fundamental interests; to ensure that drugs and devices are safe and effective while not unduly delaying the availability of safe and effective products to patients in need. This balancing of interests is seen throughout the FDA's process for clearing and approving drugs and medical devices.

⁸ CMS Medicare Learning Network. MM 6191, CR6191. October 24, 2008. Available at: <http://www.cms.hhs.gov/MLNMattersArticles/downloads/MM6191.pdf>. Accessed March 10, 2009.

⁹ See generally, Curtiss F., Contradictory Actions of Off-Lable Use of Prescription Drugs? The FDA and CMS Versus the US Department of Justice: Journal of Managed Care Pharmacy, Vol. 15, No. 2, March 2009.

¹⁰ See FDA's Mission Statement, available at www.fda.gov/opacom/morechoices.html (accessed on March 1, 2009).

The FDA is responsible for regulating the introduction of prescription drugs and medical devices into commerce.¹¹ Before a drug or device can be introduced or distributed into commerce the FDA must approve its “labeled use”.¹² For each drug or device¹³ the FDA makes a determination of its safety and efficacy for particular uses by reviewing supporting evidence submitted by the manufacturer. Or in other words, upon application to the FDA by the manufacturer, the FDA decides whether to approve or clear the particular drug for the applied “for use indication”.¹⁴

The Food Drug and Cosmetic Act, 21 U.S.C. §§ 301 et seq., (FDCA) requires that manufacturers label their products with safety warnings and directions for use.¹⁵ Over time, the FDA has come to understand this requirement as mandating that drug and device manufacturers label their product with a description of all intended uses. Thus the agency has declared “All drugs and devices must bear labeling with adequate directions for each intended use. If labeling for a drug or device fails to contain adequate directions for each intended use, the drug or device is deemed misbranded...and subject to seizure or other enforcement actions.”¹⁶ As a result it is the FDA’s position that promotion of a drug for a use that is not on-label, thereby off-label, is strictly prohibited.

¹¹ 21 U.S.C. §301 et seq.

¹² 21 U.S.C. §§355(a), 355(d).

¹³ The issues discussed in this paper apply both to drugs and devices unless clearly indicated otherwise. But because the pharmaceutical industry has had a greater number of cases addressing off-label use, the term drug will imply both drug and device throughout the remainder of this paper.

¹⁴ For medical devices the approval process is a little more complex in that it varies depending upon the risk classification of the device.

¹⁵ 21 U.S.C. §§355(a), 355(d).

¹⁶ 21 CFR § 201.5(a) (requiring directions for use to state “all conditions, purposes, or uses for which [a] drug is intended.”); see also Final Guidance on Industry Supported Scientific and Educational Articles, 62 Fed. Reg. 64074, 64075 (Dec. 3, 1997) (“The courts have agreed with the agency that section

The FDA regulates manufacturers marketing practices by prohibiting the direct promotion of products for unapproved uses. In 1997, Congress enacted Section 401 of the FDA Modernization Act (FDAMA)¹⁷, Congress created a temporary exception to the off-label marketing rule by allowing drug and device manufacturers to distribute peer reviewed research from reputable medical journals that discussed off-label uses by physicians. One of the requirements was that the manufacturers had to submit the articles to the FDA for advance review so that the FDA could approve of the new use described in the article. This off-label promotion exception expired in September 2006.

After its expiration the FDA wanted to renew the exception, but with some changes. In February 2008, the FDA issued proposed guidance that allowed manufacturers to distribute articles without prior FDA approval. According to the New York Times, the FDA had justified this loosening of the rules by claiming they never really enforced the requirements anyway. One year later, the FDA published its most recent Final Guidance, referred to as “Good Reprint Practices” which is much more permissive than any of its previous guidance. (The requirements of FDA’s Good Reprint Practices are discussed in more detail in the next section.)

The other counter factor that the FDA has had to deal with since 1998 is the legal debate lodged by the Washington Legal Foundation (WLF) about whether the FDA’s regulation of off-label marketing is a violation of manufacturer’s First Amendment rights.¹⁸ The Court has repeatedly held that the FDA’s Guidance Documents were more

¹⁷ Pub. L. No. 105-115 (Nov. 27, 1997), at § 401, codified at 21 U.S.C. § 360aaa et seq. Implementing regulations at 21 C.F.R. Part 99 (2001).

¹⁸ Wash. Legal Found. v. Friedman, 13 F. Supp.2d 51, D.D.C. (1998).

extensive than necessary to serve the asserted government interest and unduly burdened important speech.¹⁹ The WLF continues to claim that the FDA regulation of prescription drug promotion “is being conducted in a manner that routinely violates both the First Amendment and the FDA’s statutory mandate.”²⁰ And that “FDA routinely orders suppression of truthful speech, demands that manufacturers engage in corrective advertising in the absence of any evidence that consumers have been misled by supposedly misleading advertising, and violates federal administrative law by using letters (rather than established notice and comment procedures) to adopt new agency policies regarding product promotion.”²¹ It appears that WLF remains posed to challenge the FDA’s oversight of off-label and it will be interesting to see if their First Amendment challenges of FDA’s Guidance will continue.

A. Physicians Off-Label Prescribing Practices

As previously discussed, an “off-label” use of a drug is simply a use for a condition or in a manner not appearing on the FDA approved label. Once the FDA approves a prescription medication to treat a specific condition, a physician is free to prescribe the medication to treat other medical conditions that the doctor believes the drug is beneficial for the patient.²² This is true even if the FDA has not determined that the drug is safe and effective for treating a particular condition. Additionally,

¹⁹ Id. At 71-72. The court struck down the FDA’s (1) Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data, 61 Fed. Reg. 52800 (Oct. 8, 1996); (2) Guidance for Industry Funded Dissemination of Reference Texts, 61 Fed. Reg. 52800 (Oct. 8, 1996); and (3) Final Guidance on Industry Supported Scientific and Educational Activities, 62 Fed. Reg. 64074 (Dec. 3, 1997).

²⁰ Wash. Legal Foundation, Case Detail: Report on FDA First Amendment Abuses (Aug. 7, 2006), available at www.wlf.org/litigating/casedetails.asp?detail=440.

²¹ Id.

²² See 21 C.F.R. §314.54, see e.g., 59 Fed. Reg. 59820, 59821 (Nov. 18, 1994) (noting that the Agency has restated this policy on numerous occasions).

manufacturers are strictly limited in what they can communicate to physicians about off-label use. Such limitations, however, do not apply to physicians communicating with other physicians about their observations and experiences with the off-label use of a drug.

Physicians have long prescribed drugs for off-label uses. According to a 2006 analysis published in the Archives of Internal Medicine, off-label use of prescription drugs is estimated to be 21% of drug use overall.²³ And amongst psychiatric drugs, it rises to 31%, one out of three psychiatric drugs are being prescribed for a use not approved by the FDA.²⁴ Moreover, 50% of cancer drug use, 80% of pediatric use, and 80% to 90% of drugs used to treat rare diseases are prescribed “off-label.”²⁵

The National Cancer Institute, a government agency, lists on its website off-label uses of many drugs as “standard of care.” Perhaps the best known example is aspirin. For years, physicians prescribed aspirin to reduce the risk of heart attacks however, the FDA had not approved such use until 1998. While some off-label therapies are widely accepted, and doctors could be accused of malpractice if they did not prescribe the drug, others are dangerous and are not appropriate part of medical care. The FDA’s policy on “off-label” prescribing states that “a physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patient, or may otherwise vary the conditions of use from those approved in the package insert.”²⁶

B. Advantages & Disadvantages of Off-Label Use

²³ David C. Radley et al., Off-Label Prescribing Among Office Based Physicians, 166 Archives Internal Med. 1021 (2006).

²⁴ Id.

²⁵ Id.

²⁶ Supra 17.

Physicians' freedom to prescribe off-label carries important advantages. It permits innovation in clinical practice, particularly when approved treatments have failed. It offers patients and physicians earlier access to potentially available treatments and allows physicians to adopt new practices based on emerging evidence. And it can provide the only available treatments for "orphan" conditions. On the other hand, there are risks of off-label use such as: it undercuts the expectations that drug safety and efficacy have been fully evaluated; it undermines the incentives for manufacturers to conduct additional clinical studies-and may instead encourage them to game the system by seeking approval for secondary indications for which clinical trials are less complicated and or less expensive; and off-label use may discourage evidence-based practice.

Over the past several years there have been numerous conflicts about off-label use. Payers question the need to pay for products that are not proven. Physicians desire the autonomy to prescribe drugs that match individual patient need regardless of label despite the difficulties they face staying abreast of rapidly evolving evidence. The pharmaceutical and device industry seek to enlarge its market to ensure future profits and sustain future research and development. The public wants drugs and devices that are safe, evidence-based, and affordable. Consumers also want the newest therapies in times of need.

C. FDA's Good Reprint Practices

In addition to allowing doctors to prescribe drugs for "off-label" uses, the FDA has never sought to restrict the ability of third parties to publish and disseminate scientific information about "off-label" uses. The FDA has repeatedly recognized the importance

of “open dissemination of scientific and medical information regarding these treatments.” In testimony provided to Congress in 1996, the FDA’s Deputy Commissioner for Policy gave an expansive explanation of the FDA’s policy, he said:

Generally, the FDA does not prohibit the dissemination of information to health care professionals. Physicians access information about off-label uses through compendia, journal articles, continuing medical education programs, symposia, and professional meetings. Physicians also have access to a number of databases that provide information about off-label uses. For example, the National Cancer Institute’s Physician Data Query (PDQ) system is an excellent source for oncologists to obtain information about current oncologic therapies. The National Library of Medicine (NLM) offers a Medical Literature Analysis and Retrieval System (MEDLARS), which is a computerized system of databases and databanks pertinent to biomedical research and patient care. NLM currently offers free access to three databases relating to AIDS. FDA does not regulate a physician’s access to any of these types of independent off label use information-no matter how preliminary it may be. In addition, FDA does not prohibit a manufacturer from providing a physician with information about off label uses if the physician requests the information. Recently, the agency announced a proposed change to its policy with respect to the dissemination of reference texts (medical textbooks and compendia). Drug companies may distribute independent reference texts even if they contain certain information about off label uses of approved drugs, as long as the texts do not have a significant focus on an off-label use of the manufacturer supporting the dissemination

of the text. FDA recognizes that all of these sources of information can be very important to good medical practices.

Shortly after, Congress enacted Section 401 of the Food and Drug Modernization Act²⁷ (FDAMA), which allowed for the dissemination of information on unapproved uses of FDA-approved products. Under Section 401 and implementing regulation, as long as the guidelines were met, the dissemination of such materials was not viewed as evidence of intent to promote off-label.

Following the sunset of the statute in September 2006 there was no formal guidance on “good reprint practices.” The FDA published draft guidance early in 2008. On January 12, 2009 the FDA released its current views on the “dissemination of medical journal articles and medical or scientific reference publications on unapproved uses of approved drugs and approved or cleared medical devices to health care professionals and healthcare entities.”²⁸ In the Final Guidance, the FDA still encourages manufacturers to seek approval and clearance for new indications of drugs and devices, but recognizes “the important public health and policy justification” of dissemination of publications on unapproved uses. Overall, the Guidance aims to make certain that off-label articles and publications are “truthful and non-misleading.” In order to do so, FDA makes recommendations directed at the three following areas:

1. the types of publications that should be distributed

²⁷ 21 U.S.C. § 360aaa, § 551, Federal Food, Drug, and Cosmetic Act (FD&C Act). Implementing regulations were codified at 21 CFR Part 99.

²⁸ FDA Guidance for Industry: Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices in the U.S., 74 Fed. Reg. 1694, January 12, 2009 accessed at <http://www.fda.gov/oc/op/goodreprint.html>

2. the types of studies and data that it views as sufficient to support such publications
3. the manner in which the manufacturer disseminates the publication to health care professionals

As an incentive for compliance, the Guidance acts as “safe harbor” whereby a compliant manufacturer’s dissemination of publications discussing off-label uses will not be used as evidence of an intent to promote off-label use of the manufacturer’s product so long as all of the following is satisfied.

1. Types of publications

In order to meet the safe harbor, the publications must meet all of the following guidelines:

- be published by an organization that has an editorial board that uses independent experts in the given field to review, select and provide feedback,
- be peer reviewed and published in accordance with peer review procedures
- be generally available through independent distribution channels where medical textbooks and periodicals are sold,
- not be funded by, primarily distributed by, or written or edited by (or at the request of) the manufacturer of the product that is subject to the article, not be edited or significantly influenced by a drug or device manufacturer or by any individuals having a financial relationship with these manufacturers

2. Studies and Data

In addition to the above, the information that the publication is based must:

- reflect adequate, well-controlled, and scientifically-sound clinical investigations
- not be false or misleading
- not pose a significant risk to the public health, if relied upon

3. Manner of Distribution

Finally, the Guidance addresses the manner in which manufacturers should disseminate off-label publications. The information must:

- be an unabridged copy or reprint that is unmarked and unaltered by the manufacturer
- be accompanied by: approved labeling; a comprehensive bibliography of publications related to the unapproved use (when such information exists); and a representative publication reaching a contrary or different conclusion regarding the unapproved use (when such information exists)
- be distributed separately from information that is promotional in nature
- include a disclosure statement (prominently and permanently affixed to the publication) stating: that the uses described have not been approved or cleared by the FDA; the manufacturer's interest at stake; any author with a known financial interest in the product or manufacturer, the affiliation of the author, and the nature of the financial interest; any person known to have funded the study; and any significant known risks of the unapproved use that are not discussed in the publication

As a whole the Guidance focuses more on disclosure and clarity of all relevant information than the draft guidance, but it is still less stringent than the FDA's prior review rules under the FDAMA. Given this perceived relaxation of the previous rules, some lawmakers, such as Representative Henry Waxman (D-CA), has strongly opposed the regulation and has been encouraging further action by the Obama Administration.²⁹

II. Summary of Recent Enforcement Actions by the Department of Justice

Enforcement of drug marketing used to be primarily conducted through the FDA in an administrative setting; this is no longer the case. Recent investigations into drug marketing and promotion are now investigated by the DOJ with the assistance of the FDA. The government's position is that off-label marketing, rather than independent medical judgment, "causes" a physician to prescribe an unapproved prescription drug and therefore when the provider submits a claim for payment for such drug, the claim is "false" under the Federal False Claims Act.³⁰

Off-label marketing continues to be an area in constant flux due both to increasing enforcement activities and to continual regulatory changes. Although it is permissible for physicians to prescribe drugs and medical devices off-label, the FDA and various law enforcement agencies take the position that it is illegal for manufacturers to promote their drugs and devices for such purposes. The federal government has been aggressively pursuing off-label marketing cases in the past several years. Already in 2009, the

²⁹ Original statement found at Letter from Henry Waxman, Chairman, House of Representatives Committee on Oversight and Government reform (Nov. 30, 2007) available at <http://oversight.house.gov/documents/20071130102744.pdf>, additional comments found in various recent news articles.

³⁰ 31 U.S.C. §3729(a); 64 Fed. Reg. 47099, 47104 at § 85.3(a)(9) (Aug. 30, 1999).

Department of Justice ("DOJ") has announced nearly \$3 billion in settlements of claims involving off-label marketing. Due to these huge settlements and to a variety of other factors, off-label marketing has become a subject of intense public scrutiny.

Although claims under the FCA that typically result in the large settlements and fines that feature prominently in the press and in discussions of these cases, other laws also serve as the basis for off-label marketing claims and often are brought alongside FCA claims. For example, many FCA actions are in conjunction with charges of "misbranding" or of the introduction of an "unapproved" drug into interstate commerce in violation of the Food, Drug, and Cosmetic Act ("FDCA"). In addition, parties have pursued both SEC and RICO based claims. Finally, off-label marketing claims are often related to, and inextricably intertwined with, alleged violations of the Anti-Kickback Statute ("AKS").

A. Enforcement Actions Against Pharmaceutical Companies

Eli Lilly - Zyprexa (2009) - \$1.4 Billion

In January 2009, Eli Lilly agreed to a settlement with the DOJ related to its off-label marketing of the drug Zyprexa that included, at that time, the largest criminal fine ever paid in a health care case.³¹ The \$515 million criminal fine and a \$100 million forfeiture of assets combined with an \$800 million civil false claims reimbursement (\$438 million to the federal government and \$361 million to the state governments) for a total criminal and civil settlement of over \$1.4 billion. In addition to the financial portion

³¹ Press Release, U.S. Department of Justice, Eli Lilly and Company Agrees to Pay \$1.415 Billion to Resolve Allegations of Off-Label Promotion of Zyprexa (January 15, 2009), #09-038, *available at* <http://www.usdoj.gov/opa/pr/2009/January/09-civ-038.html>.

of the settlement, Lilly pled guilty to a misdemeanor criminal charge of distributing misbranded drugs with inadequate instructions for use and agreed to a 5-year Corporate Integrity Agreement ("CIA").

The agreement settled four FCA *qui tam* actions charging Lilly with promoting Zyprexa, an anti-depressant, off-label for treatment of dementia, agitation, and aggression in elderly patients. Specifically, Lilly is said to have expended significant resources marketing the drug both to nursing homes and to assisted-living facilities for Alzheimer-related off-label uses, and to primary-care physicians who had virtually no on-label use for Zyprexa. In addition, Lilly allegedly created marketing materials for off-label uses, trained its marketing staff to avoid the legal issues surrounding off-label uses, and encouraged its sales personnel to promote Zyprexa off-label.

Pfizer - Bextra (2009) - \$2.3 Billion

Shortly after the Eli Lilly settlement, Pfizer agreed to an even larger settlement with the DOJ.³² Although the details of the agreement are not yet known, it involved, in part, the alleged promotion of Bextra, an anti-inflammatory drug, for non-approved purposes such as surgical pain. The FDA specifically rejected the treatment of surgical pain as an accepted indication due to safety concerns arising from a study showing excess cardiovascular events in patients who used Bextra after a coronary artery bypass.

³² Sarah Rubenstein, *Pfizer Takes \$2.3 Billion Charge Linked to Bextra Probe*, Wall Street Journal: Health Blog, January 26, 2009, available at <http://blogs.wsj.com/health/2009/01/26/pfizer-takes-23-billion-charge-linked-to-bextra-probe/>.

In addition to the corporate crimes, a Pfizer company manager individually pled guilty to violating the FDCA for marketing unapproved uses and dosages of Bextra.³³ The DOJ stated that the manager was aware of the FDA safety concerns regarding the off-label use and encouraged a sales team of over 100 employees to promote it for exactly that purpose while also encouraging the sales team to make false or unsubstantiated safety and efficacy claims. The manager faces up to six months in prison and a maximum fine of \$100,000.

Cephalon - Actiq, Gabitril, & Provigil (2008) - \$425 Million

In November of 2008, biopharmaceutical manufacturer Cephalon entered into a settlement agreement with the DOJ for \$425 million to resolve allegations of off-label promotion of three drugs, Actiq, Gabitril, and Provigil.³⁴ The agreement consisted of a \$40 million criminal fine and a \$10 million forfeiture of assets. In addition, Cephalon paid \$375 million to settle civil claims. Cephalon also pled guilty to distribution of misbranded drugs, a misdemeanor violation of the FDCA, and entered into a CIA with the OIG.

Cephalon's alleged impermissible off-label promotion involved marketing Actiq (approved for extreme cancer-related pain) for general pain including migraines, Gabitril (approved as an anti-epileptic) for anxiety and insomnia, and Provigil (approved for

³³ Press Release, U.S. Department of Justice, Federal Bureau of Investigation: Boston Field Division, Pharmaceutical Company Manager Pleads Guilty to Off-Label Marketing (March 30, 2009), *available at* <http://boston.fbi.gov/dojpressrel/pressrel09/bs033009.htm>
³⁴ Press Release, U.S. Department of Justice, Biopharmaceutical Company, Cephalon, to Pay \$425 Million & Enter Plea to Resolve Allegations of Off-Label Marketing (Sept. 29, 2008), #08-860, *available at* <http://www.usdoj.gov/opa/pr/2008/September/08-civ-860.html>.

narcolepsy-related conditions) for fatigue. The government found that more than 80% of the sales of these three drugs were for off-label purposes. The allegedly impermissible practices involved training sales personnel to ignore FDA labeling restrictions, promoting the drugs for off-label uses, and marketing to practitioners with little exposure to patients requiring these drugs for FDA-indicated uses. In addition, Cephalon allegedly paid medical professionals to speak about and to author studies on the off-label uses while simultaneously contributing millions of dollars to educational programs featuring this information.

Specialty Distribution Services/Express Scripts - Human Growth Hormone
(2007) - \$10.5 Million

In September 2007, Specialty Distribution Services ("SDS"), a subsidiary of Express Scripts, entered into a 36-month Deferred Prosecution Agreement ("DPA") with the DOJ for its alleged off-label distribution of human growth hormone ("HGH").³⁵ As part of the agreement, SDS paid a \$10.5 million fine, agreed to change certain business practices, and committed to cooperate with any future investigations. The HGH in question was approved by the FDA for treatment of growth-related diseases in children, but SDS is alleged to have knowingly distributed the product for off-label uses including athletic performance enhancement, cosmetic purposes, and anti-aging uses.

³⁵ Press Release, U.S. Department of Justice, U.S. Attorney's Office: Dist. of Mass., Express Scripts Subsidiary Agrees to Deferred Prosecution for Illegal Distribution of Human Growth Hormone (Sept. 10, 2007), *available at* <http://www.usdoj.gov/usao/ma/Press%20Office%20-%20Press%20Release%20Files/Sept2007/Express%20Scripts.html>.

It is important to note that the DOJ pursued SDS for off-label distribution even though SDS was not participating in the same comprehensive, expensive, and systematic off-label marketing plans seen in other cases. This heightened scrutiny is due in part to the special treatment of HGH under the FDCA, which disallows physicians from prescribing HGH for any off-label use and eases the burden of proof for prosecuting HGH distribution cases. In addition, some added scrutiny likely comes from publicity surrounding athlete's and celebrities' uses of HGH for performance enhancing and cosmetic purposes.

Orphan Medical/Jazz Pharmaceuticals - Xyrem (2007) - \$20 Million

In July 2007, Jazz Pharmaceuticals, in conjunction with its subsidiary Orphan Medical, agreed to a \$20 million settlement of claims that it marketed the drug Xyrem for off-label purposes.³⁶ Xyrem, more commonly known as "GHB" or the "date-rape" drug, is approved for treating narcolepsy-related conditions in adults. Orphan agreed to pay, and Jazz to guarantee, a criminal fine of \$5 million, criminal restitution of \$12.2 million, and a civil settlement of \$3.75 million. In addition, Orphan pled guilty to felony misbranding under the FDCA and Jazz entered into a CIA with the OIG. One Orphan sales manager pled guilty to a felony count of introducing a misbranded drug into interstate commerce. An Orphan-paid psychiatrist also was indicted, but it still fighting the charge.

³⁶ Press Release, U.S. Department of Justice, U.S. Attorney's Office: E. Dist. of N.Y., Jazz Pharmaceuticals, Inc., Agrees to Pay \$20 Million to Resolve Criminal and Civil Allegations in "Off-Label" Marketing Investigation (July 13, 2007), *available at* <http://www.usdoj.gov/usao/nye/pr/2007/2007jul13a.html>.

To advance the off-label uses, Orphan allegedly promoted the drug in children, minimized its side effects, and encouraged prescription of the drug for such off-label uses such as fatigue, insomnia, and depression. Specifically, Orphan sales staff are alleged to have marketed to physicians not treating narcolepsy patients and distributed written materials regarding off-label uses not in compliance with FDA rules. In addition, Orphan paid the indicted psychiatrist to participate in speaking engagements discussing the off-label uses of Xyrem during which he made misleading statements about the off-label uses, downplayed the dangers of the drug, and gave advice to physicians on how to avoid off-label reimbursement restrictions.

Purdue Frederick - OxyContin (2007) - \$635 Million

In May 2007, Purdue Frederick, along with three of its executives, pled guilty to misbranding of the drug OxyContin.³⁷ Of the \$635 million settlement, the company will pay \$600 million and the executives will pay \$35 million. The \$600 million involves a criminal fine and forfeiture, payments to federal and state healthcare programs, a set aside for private civil claims, and payments to specific Virginia state programs. The three executives will each pay a criminal fine and an individual amount to the Virginia Medicaid Fraud Control Unit. The company pled guilty to felony misbranding and the executives to misdemeanor misbranding.

Purdue Frederick's impermissible actions were not typical of those off-label cases involving promoting a drug for a non-indicated use. Instead, the company, in pleading

³⁷ Press Release, U.S. Department of Justice, U.S. Attorney's Office: W. Dist. of Va., The Purdue Frederick Company, Inc. and Top Executives Plead Guilty to Misbranding OxyContin; Will Pay Over \$600 Million (May 10, 2007), *available at* http://www.usdoj.gov/usao/vaw/press_releases/purdue_frederick_10may2007.html.

guilty to the FDCA-related charges, agreed that it made false claims that OxyContin was less addictive, less subject to abuse, and less likely to cause withdrawal symptoms than other pain medications. These claims were not approved by the FDA and were not supported by any medical research. The government alleged that Purdue Frederick misbranded Oxycontin in three specific ways: 1) sales representatives falsely told health care providers, through exaggerated graphs and presentations, that the drug was less euphoric and less addictive; 2) employees drafted an article about a study on OxyContin and distributed it to health care providers in an attempt to mislead them with its content; and 3) sale representatives misconstrued terminology on the drug's label to imply it had less abuse and addiction potential than it truly did.

Medicis - Loprox (2007) - \$9.8 Million

In May 2007, Medicis settled allegations that it falsely submitted claims through its off-label promotion of the drug Loprox.³⁸ In particular, Loprox was approved by the FDA for treatment of skin disorders in adults, but Medicis supposedly marketed it for pediatric use through having its sales personnel target pediatricians and promote Loprox as a treatment for diaper rash. Medicis agreed to settle the FCA *qui tam* action for \$9.8 million.

Pharmacia & Upjohn Company/Pfizer - Genotropin (2007) - \$35 Million

In April 2007, Pharmacia, a Pfizer subsidiary, simultaneously pled guilty to offering a kickback and entered into a Deferred Prosecution Agreement for off-label

³⁸ Press Release, U.S. Department of Justice, Medicis Pharmaceutical To Pay U.S. \$9.8 Million to Resolve False Claims Allegations (May 8, 2007), # 07-336, *available at* http://www.usdoj.gov/opa/pr/2007/May/07_civ_336.html.

promotion of its drug, Genotropin.³⁹ Of the \$35 million agreement, \$15 million was a monetary penalty attributable to the off-label marketing portion of the settlement. In addition to the penalty and 36-month DPA, Pharmacia agreed to provide employees with specific training and to cooperate with ongoing investigations. Genotropin was approved for treatment of childhood growth diseases, but was marketed for athletic performance, anti-aging, and cosmetic uses. Although Pharmacia's conduct pre-dated Pfizer's acquisition of the company, Pfizer was the entity that disclosed the conduct to the government.

Schering-Plough - Temodar & Intron (2006) - \$435 Million

In August 2006, Schering-Plough pled guilty to felony conspiracy to make false statements to the FDA arising from a *qui tam* action based, in part, on its off-label marketing of the drugs Temodar and Intron.⁴⁰ Along with \$435 million in criminal and civil portions of the settlement, Schering Sales Corporation, a subsidiary of Schering-Plough, was permanently excluded from federal health care programs. The off-label claims involve Schering-Plough's drugs Temodar and Intron, both approved for very specific types of cancer, being promoted for non-approved types of cancer as well as for other diseases.

³⁹ Press Release, U.S. Department of Justice, Federal Bureau of Investigation: Boston Field Division, Pfizer Subsidiary Agrees to Plead Guilty for Offering Kickback and Pay \$19.68 Million Criminal Fine; Second Subsidiary Agrees to Pay Additional \$15 Million Penalty to Resolve Allegations of Illegal Promotion of Human Growth Hormone (April 6, 2007), *available at* <http://boston.fbi.gov/dojpressrel/pressrel07/kickbackplea040207.htm>.

⁴⁰ Press Release, U.S. Department of Justice, U.S. Attorneys Office: Dist. of Mass., Schering to Pay \$435 Million for the Improper Marketing of Drugs and Medicaid Fraud (August 26, 2006), *available at* <http://www.usdoj.gov/usao/ma/Press%20Office%20-%20Press%20Release%20Files/Schering-Plough/press%20release.pdf>.

After initially addressing off-label concerns, Schering-Plough assured FDA officials that these were isolated occurrences and that such occurrences were being addressed internally. Prosecutors allege that, in reality, the off-label activities were part of a centrally-run national marketing plan that included improper gifts to physicians, improper distribution of clinical literature, and various other improper relationships. Due to the allegedly egregious conduct combined with the company's mistatements, the DOJ pursued further actions and instituted harsh penalties.

InterMune - Actimmune (2006) - \$37 Million

In October 2006, biopharmaceutical firm InterMune agreed to a \$37 million settlement with the DOJ regarding its alleged off-label marketing of Actimmune.⁴¹ Specifically, Actimmune was promoted for treatment of idiopathic pulmonary fibrosis, even though it was not FDA-approved for such a use. Although InterMune conducted a clinical trial for this use, it failed to establish a statistically significant benefit. Nonetheless, the company distributed a press release characterizing the study as showing beneficial results. Of the \$37 million settlement, \$30 million will go to federal health care programs and \$7 million to state Medicaid programs. InterMune also entered into a two-year DPA in connection with the felony charges under the FDCA of promoting Actimmune with the intent to defraud or mislead. Finally, the company entered into a CIA with the OIG.

⁴¹ Press Release, U.S. Department of Justice, Biopharmaceutical Firm InterMune to Pay U.S. Over \$36 Million for Illegal Promotion and Marketing of Drug Actimmune (Oct. 26, 2006), # 06-728, *available at* http://www.usdoj.gov/opa/pr/2006/October/06_civ_728.html.

In addition to the company itself, in 2008, InterMune's CEO was indicted for wire fraud and for felony FDCA charges for his involvement in the off-label marketing of Actimmune and the aforementioned press release.⁴² The CEO is alleged not only to have marketed Actimmune for off-label uses, but also to have made false and misleading claims regarding the drug's safety and efficacy for such uses and to have caused the distribution of misleading information related to these claims. The wire fraud and felony FDCA charges are punishable by both criminal fines and imprisonment.

Eli Lilly - Evista (2005) - \$36 Million

In December 2005, in a settlement dwarfed by its later Zyprexa settlement, Eli Lilly pled guilty to misbranding under the FDCA for its illegal promotion of the drug Evista.⁴³ For the criminal portion, Lilly agreed to pay a \$6 million criminal fine and a \$6 million criminal forfeiture. For the civil portion, Lilly agreed to pay \$24 million in equitable disgorgement and to enter into a consent decree of permanent injunction, the terms of which are similar to a CIA.

Lilly allegedly marketed Evista, which is approved for osteoporosis, for the prevention of breast cancer, and for the reduction of risk of cardiovascular disease. Although the Evista label included no such uses and these uses were specifically rejected by the FDA, Lilly's marketing plans and promotions allegedly touted these off-label uses

⁴² Press Release, U.S. Department of Justice, Federal Bureau of Investigation: San Francisco Field Division, Former Intermune CEO W. Scott Harkonen Indicted for Wire Fraud and FDA Violations (March 18, 2008), *available at* <http://sanfrancisco.fbi.gov/dojpressrel/2008/sf031808.htm>.

⁴³ Press Release, U.S. Department of Justice, Eli Lilly Company to Pay U.S. \$36 Million Relating to Off-Label Promotion (Dec. 21, 2005), # 05-685, *available at* http://www.usdoj.gov/opa/pr/2005/December/05_civ_685.html.

and Lilly's business plan noted these uses as a potential for counteracting disappointing revenue from Evista. The impermissible sales activities involved conducting one-on-ones with physicians regarding off-label uses, sending unsolicited medical letters promoting off-label uses, organizing events discussing off-label uses, and training sales representatives to tout off-label uses.

Serono Labs - Serostim (2005) - \$704 Million

In October 2005, Serono agreed to pay \$704 million in settlement of DOJ claims related to its marketing and promotion of Serostim and a biomedical impedance analysis device manufactured by RJL Sciences.⁴⁴ The settlement includes a \$137 million criminal fine and \$567 million in civil liabilities. In addition, Serono pled guilty to conspiracy with RJL Sciences to promote its device without FDA approval in order to increase the market for such devices, and thus to increase the market for Serostim. Finally, Serono Labs will be excluded from federal health care programs for five years and its U.S. subsidiary will be under a strict five-year CIA.

Serono Labs partnered with RJL Sciences to increase the market for RJL's device for evaluating body cell mass as an indicator in the diagnosis of AIDS "wasting syndrome." In turn, Serono intended to promote the device and the resulting diagnoses as a way to increase the market for its drug Serostim, which is prescribed for AIDS wasting syndrome. But, not only was the device not approved by the FDA, but the device

⁴⁴ Press Release, U.S. Department of Justice, Serono to Pay \$704 Million for the Illegal Marketing of AIDS Drug (Oct. 17, 2005), # 05-545, *available at* http://www.usdoj.gov/opa/pr/2005/October/05_civ_545.html.

measured only body cell mass, which is not an accepted method of diagnosing AIDS wasting.

Warner-Lambert/Pfizer - Neurontin (2004) - \$430 Million

In May 2004, Warner-Lambert, a subsidiary of Pfizer, pled guilty to two felony counts of violating the FDCA for misbranding its drug Neurontin and agreed to pay \$430 million as part of the settlement of these charges.⁴⁵ The settlement involves a criminal fine of \$240 million and \$190 million in civil liabilities. In addition, even though the actions predated Pfizer's acquisition of the company, Pfizer agreed to comply with the terms of a CIA.

The case involved Warner-Lambert's marketing of the anti-epileptic drug Neurontin for a variety of off-label uses including bipolar disorder, ADD, pain disorders, and others. Allegedly, Warner-Lambert did this by promoting the drug as the sole treatment for epileptic seizures even though the FDA rejected monotherapy as an indication, promoting the drug for bipolar disorder when studies showed no effectiveness, encouraging sales representatives to promote off-label uses, and allowing these representatives to make false and misleading statements regarding these uses.

⁴⁵ Press Release, U.S. Department of Justice, Warner-Lambert to Pay \$430 Million to Resolve Criminal & Civil Health Care Liability Relating to Off-Label Promotion (May 13, 2004), # 04-322, *available at* http://www.usdoj.gov/opa/pr/2004/May/04_civ_322.htm.

Genentech - Protropin (1999) - \$50 Million

In April 1999, predating the later off-label HGH settlements, Genentech settled with the DOJ on its marketing of the HGH Protropin.⁴⁶ In addition to pleading guilty to a misdemeanor violation of the FDCA, Genentech paid a \$30 million criminal fine and \$20 million in civil restitution to Medicaid and to CHAMPUS. Although Genentech admitted to promoting Protropin for off-label use in children who were not growth hormone deficient, the government, as part of the settlement agreement, acknowledged that these practices ended in 1994 when the company instituted a more strict compliance program.

Bristol-Myers Squibb - Abilify (2007) - \$515 Million

In September 2007, Bristol-Myers Squibb agreed to pay \$515 million dollars to settle various civil allegations arising out of the alleged off-label marketing and pricing of the drug Abilify.⁴⁷ The \$515 million settlement resolves seven *qui tam* actions and includes payments of \$328 million to the federal government, \$187 million to state Medicaid programs, and \$124,000 to certain Public Health Service entities. Additionally, Bristol-Myers entered into a five-year CIA.

The settlement covers a wide range of allegations including illegal kickbacks, fraudulent inflation of price, misreporting of best price, and off-label marketing. The off-label marketing claims in particular arise out of the promotion of Abilify beyond its

⁴⁶ Tamar Nordenberg, *Maker of Growth Hormone Feels Long Arm of Law*, FDA Consumer, Vol. 33, (Sept. 1999).

⁴⁷ Press Release, U.S. Department of Justice, U.S. Attorney's Office: Miami Field Division, Bristol-Myers Squibb to Pay More than \$515 Million to Resolve Allegations of Illegal Drug Marketing and Pricing (Sept. 28, 2007), *available at* <http://miami.fbi.gov/dojpressrel/pressrel07/mm20070928a.htm>.

approved uses for adult schizophrenia and bipolar disorder. Bristol-Myers allegedly marketed Abilify for children and for the elderly as a treatment for dementia and psychosis. Bristol-Myers achieved this by marketing to child psychologists and to pediatricians. On the geriatric side, it allegedly established a sales force specifically for nursing homes and for long-term care facilities.

Otsuka - Abilify (2008) - \$4 Million

In conjunction with the Bristol-Myers Squibb settlement, Otsuka agreed to pay a \$4 million civil settlement including \$2.3 million to the federal government and \$1.7 million to state Medicaid programs.⁴⁸ Otsuka also entered into a CIA with the OIG. Otsuka developed Abilify, the drug in the Bristol-Myers settlement, and entered into an agreement with Bristol-Myers for co-promotion of the drug through Otsuka sales representatives and Bristol-Myers sales managers. As such, the claim arose out of the same off-label marketing allegations explained above.

Cell Therapeutics - Trisenox - \$10.5 Million

In April 2007, Cell Therapeutics agreed to pay \$10.5 million to settle a *qui tam* action based on the alleged off-label marketing of its drug Trisenox.⁴⁹ The FDA approved Trisenox only for a very specific type of cancer, acute promyelocytic leukemia, but Cell Therapeutics allegedly marketed the drug for various other types of cancer. In

⁴⁸ Press Release, U.S. Department of Justice, Otsuka to Pay More than \$4 Million to Resolve Off-Label Marketing Allegations Involving Abilify (March 27, 2008), # 08-244, available at http://www.usdoj.gov/opa/pr/2008/March/08_civ_244.html.

⁴⁹ Press Release, U.S. Department of Justice, Cell Therapeutics, Inc. to Pay United States \$10.5 Million to Resolve Claims for Illegal Marketing of Cancer Drug (April 17, 2007), # 07-258, available at http://www.usdoj.gov/opa/pr/2007/April/07_civ_258.html.

addition, the settlement resolved a variety of related allegations involving kickbacks to prescribing physicians for these off-label uses.

B. Actions Against Medical Device Companies

Orthofix - Physio-stem (2003) - \$1.6 Million

In September 2007, Orthofix, a medical device manufacturer, agreed to a settlement of \$1.6 million with the DOJ.⁵⁰ The settlement resolves an FCA *qui tam* action regarding Orthofix's alleged off-label promotion of its device, the Physio-stem. The FDA approved the Physio-stem for healing fractures on long bones, such as arms and legs. Orthofix, however, allegedly promoted the device for unapproved use on the cervical spine.

In addition to the abovementioned cases involving more traditional off-label uses of pharmaceuticals and medical devices, there are also a variety of cases that relate to the labeling of medical devices, but do not fall into quite the same subset as the pharmaceutical off-label marketing settlements. Briefly, some of these cases include:

Numed - CP Stent (2007) - \$4.5 Million

In July 2007, Numed pled guilty to distributing medical devices not approved by the FDA. The allegations involved distribution of the CP Stent.⁵¹ Numed admitted that it

⁵⁰ Press Release, U.S. Department of Justice, Texas-Based Medical Device Manufacturer to Pay U.S. \$1,575,000 to Resolve False Claims Allegations (Sept. 16, 2003), # 03-222, available at http://www.usdoj.gov/opa/pr/2003/September/03_civ_222.htm.

⁵¹ Press Release, U.S. Department of Justice, U.S. Attorney's Office: Dist. of Del., Medical Device Manufacturer Pleads Guilty to Healthcare Crime; Agrees to Pay Multi-Million Dollar Fine for Failure to Obtain FDA Approval (July 30, 2007), available at

distributed the CP Stent without first obtaining the necessary pre-market approval or pre-market clearance. Numed agreed to pay a criminal fine of \$2.3 million and to pay \$2.2 million to Johns Hopkins University to fund a clinical trial for the CP Stent. In addition, if the clinical trial leads to approval/clearance, Numed agreed to provide the CP Stents at no cost to any health care provider in the U.S. who requests the device for approved uses.

Serono Labs - Serostim (2005) - \$704 Million

See above discussion under "Actions Against Pharmaceutical Companies" Section. The Serono case involved the marketing of Serostim in conjunction with a device not approved by the FDA and not effective for the marketed purpose.

Augustine Medical - Warm-Up (2004) - \$12.7 Million

In September 2004, Augustine Medical and five former employees, including the company's CEO, CFO, and GC, pled guilty to various healthcare-related fraud counts arising from the approval and marketing of its device, the Warm-Up wound heating device.⁵² Augustine paid a fine of \$5.2 million, a civil penalty of \$7.4 million, and entered into a five-year probation period (Augustine's parent, Arizant, was also required to enter a CIA). The employees, four former executives and a reimbursement consultant, were required to pay fines ranging from \$100,000 to \$2 million in addition to non-monetary penalties ranging from probation to confinement.

<http://www.usdoj.gov/usao/de/press/2007/7-30-07%20Medical%20Device%20Manufacturer%20Pleads%20Guilty.pdf>.

⁵² Press Release, U.S. Department of Justice, U.S. Attorney's Office: S. Dist. of Ill., Augustine Medical Sentenced to \$5,249,910 Fine (Sept. 8, 2004), *available at* <http://www.integrityguard.org/corp/newsevents/pressreleases/2004/2004-09-08.html>.

The charges arose out of Augustine's decision to obtain FDA 510(k) approval for its device as substantially equivalent to existing wound dressings. In reality, the device was a more complex system that included both expensive durable medical equipment and disposable elements. After approval, the device did not become profitable because it was costly, but was reimbursed in a way that did not that reflect the cost of the device.

As a result, Augustine and its employees undertook extensive action to conceal the true nature of the device (and to prevent reimbursement denials) by encouraging providers not to contact CMS or insurers regarding reimbursement for the device, instructing providers to miscode the device, representing that the device was covered in ways that it was not, and other overt acts of conspiracy and fraud.

Bard - Catheter (1994) - \$61 Million

In November 1993, C.R. Bard pled guilty to violating the FDCA by distributing adulterated heart catheter devices and agreed to pay \$61 million.⁵³ The FDA labeling of the device stated it could not be turned more than one rotation in the same direction, but Bard sales personnel marketed the device as able to be rotated up to 15 times. Marketing materials specifically promoted this off-label use and the sales force, although aware of the label, were not told the reason for the restriction. Physicians then used the catheter in this way and several experienced failure and breakage of the device during use. As a result, the government found that Bard made changes in the use of the device without seeking new approvals from the FDA.

⁵³ Brian Boney, *C.R. Bard pleads guilty, faces \$61 million product settlement*, Health Industry Today, Nov. 1993, available at http://findarticles.com/p/articles/mi_m3498/is_n11_v56/ai_14649506/.

C. Pending Matters

In addition to the various cases and settlements mentioned above, there are several ongoing off-label marketing investigations that have been made public. These particular matters relate to both pharmaceutical and medical device companies. The two matters described below exemplify many pending actions. The Gilead Sciences action is unique because it involves a lawsuit brought by shareholders of the corporation through the SEC rather than under the FCA. The Medtronic lawsuit is important because it demonstrates another, more traditional off-label case as it relates to a large medical device company. Note that in addition to these two lawsuits, there are a variety of other pending actions including Par (Megace), Scios/Johnson & Johnson (Natrecor), Forest (Celexa and Lexapro), and Johnson & Johnson (Risperdal).

Gilead Sciences - Viread

The case against Gilead Sciences regarding its drug Viread is unique when compared to all the other cases previously discussed. Rather than being based on FDA claims, this is a securities fraud action brought by a group of Gilead shareholders.⁵⁴ The lawsuit accuses the company of misleading investors by representing that demand for Viread was strong without disclosing that this strength was, in large part, derived from the off-label marketing of the drug. The initial case was dismissed, but on appeal the court found that the action could proceed. The case has not been adjudicated on the merits, but it presages a possible new wave of off-label marketing cases.

Medtronic - Infuse

⁵⁴ *In re* Gilead Sciences Securities Litigation, 536 F.3d 1049 (9th Cir. 2008).

In November of 2008, Medtronic reported that the DOJ was investigating the company for the off-label use of its Infuse spinal implant.⁵⁵ The implant uses a bioengineered protein to incite bone growth and is commonly used to fuse vertebrae. Infuse is FDA-approved for use only in the lumbar region of the back, but physicians apparently use it frequently in other areas of the spine including the cervical spine. The DOJ probe, initiated by a whistleblower suit, is ongoing.

III. Conclusion

Historically, restrictions on marketing that is not misleading have been successfully challenged as infringements of commercial free speech. As a result, the FDA may be further conceding to drug manufacturers the responsibility for regulating their own off-label marketing practices. The agency may also believe that its limited resources can be put to better or more effective use in confronting other ongoing challenges. The Department of Justice, however, is strictly enforcing appropriate off-label promotion and is showing no signs of lightening up. Perhaps this approach is the right mix of liberty and scrutiny that will be best for public health, advancements in medical technology, and use of limited FDA resources.

⁵⁵ *Feds Probe Unapproved Use of Medtronic Bone Stimulator*, Wall Street Journal: Health Blog, Nov. 19, 2008, available at <http://blogs.wsj.com/health/2008/11/19/feds-probe-unapproved-use-of-medtronic-bone-stimulator/tab/print/>.