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# ARTICLES

## “There’s Danger Here, Cherie!”<sup>1</sup>

### LIABILITY FOR THE PROMOTION AND MARKETING OF DRUGS AND MEDICAL DEVICES FOR OFF-LABEL USES

*Richard C. Ausness*<sup>†</sup>

#### I. INTRODUCTION

Physicians often prescribe prescription drugs and other medications for uses that are not approved by the Food and Drug Administration (“FDA”), and such “off label” prescription is widely accepted within the medical community as a legitimate form of treatment.<sup>2</sup> However, the federal government discourages off-label prescription and use in various ways. For example, the FDA restricts the dissemination of information by drug companies about potential off-label therapies.<sup>3</sup> In addition, federally funded health insurance programs such as Medicaid do not reimburse health care providers for off-label uses.<sup>4</sup> Because drug companies make large profits from off-label prescriptions, they are often tempted to illegally promote off-label uses of their products or to encourage health care providers to defraud the federal government by seeking reimbursement for off-label uses. This conduct is exceedingly risky and has cost drug companies hundreds of millions of dollars in

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<sup>1</sup> Harry Caray, legendary sportscaster for the Chicago Cubs baseball club, often exclaimed, “There’s danger here, Cherie,” when a home-run hitter for the opposing team stepped up to the plate.

<sup>2</sup> See *infra* text accompanying notes 9-16.

<sup>3</sup> See *infra* Part II.B.

<sup>4</sup> 42 U.S.C. §§ 1396b(i)(10), 1396r-8(k)(3) (2000).

finances and civil penalties. Moreover, the current federal policy with respect to off-label use not only threatens the pocketbooks of drug companies, but also adversely affects public health by discouraging drug companies from publicizing promising off-label therapies. A revision of the current policy is urgently needed.

An off-label use is one that is not provided for on the product's FDA-approved labeling.<sup>5</sup> A doctor makes an off-label prescription when he or she prescribes a drug or medical device to treat a medical condition other than the one the drug or device was approved to treat.<sup>6</sup> Off-label prescription also involves using a different method of applying the treatment as well as prescribing a drug or device to patient groups other than those for whom the FDA approved it.<sup>7</sup> In addition, off-label use includes prescriptions for drug dosages that are different from the recommended dosage or for periods that exceed the recommended use in the labeling.<sup>8</sup>

Off-label uses are not necessarily unusual or experimental.<sup>9</sup> In fact, they are widely accepted within the medical community and may sometimes be the most effective treatment for certain types of medical conditions.<sup>10</sup> It is estimated that between twenty and sixty percent of all prescriptions are for off-label uses.<sup>11</sup> For example, a large percentage of prescriptions for pediatric use are off-label because many drugs are not tested or approved for use by children.<sup>12</sup> Off-label uses are also common in cancer therapy and are often considered to be among the most effective treatments.<sup>13</sup> Off-label uses are even

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<sup>5</sup> Stephanie Greene, *False Claims Act Liability for Off-Label Promotion of Pharmaceutical Products*, 110 PENN. ST. L. REV. 41, 43 (2005).

<sup>6</sup> 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, 189 (1999).

<sup>7</sup> Lars Noah, *Constraints on the Off-Label Uses of Prescription Drug Products*, 16 J. PROD. & TOXICS LIAB. 139, 141 (1994).

<sup>8</sup> Elizabeth A. Weeks, *Is It Worth the Trouble? The New Policy on Dissemination of Information on Off-Label Use Under the Food and Drug Administration Modernization Act of 1997*, 54 FOOD & DRUG L.J. 645, 647 (1999).

<sup>9</sup> James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions*, 53 FOOD & DRUG L.J. 71, 72 (1998).

<sup>10</sup> See Martin Page, *CBER Status on Reform Initiatives: Industry Reactions and Comments*, 52 FOOD & DRUG L.J. 193, 195 (1997).

<sup>11</sup> Michael I. Krauss, Essay, *Loosening the FDA's Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, 4 GEO. MASON L. REV. 457, 472 (1996).

<sup>12</sup> Salbu, *supra* note 6, at 193.

<sup>13</sup> William L. Christopher, *Off-Label Drug Prescription: Filling the Regulatory Vacuum*, 48 FOOD & DRUG L.J. 247, 248-49 (1993).

more prevalent in the treatment of AIDS, where between ninety and one hundred percent of applications are thought to be off-label.<sup>14</sup>

Courts have repeatedly held that certain off-label uses are legitimate forms of therapy.<sup>15</sup> The FDA has also tacitly recognized that off-label uses are legitimate.<sup>16</sup> Nevertheless, the FDA severely restricts the ability of drug manufacturers to promote off-label uses for their products.<sup>17</sup> Thus, drug companies are forced to circumvent, or even violate, the law if they wish to inform physicians about beneficial off-label therapies (and make money from the increased sales of their products). The drug companies that cross the line and get caught face substantial civil and criminal liability. This Article concludes that the current FDA policy should be revised because it encourages criminal behavior on the part of pharmaceutical companies and deprives physicians of potentially useful information about new and useful treatments.

Part II examines the FDA's drug and medical device approval processes, as well as its regulation of the promotion of off-label uses under the Food and Drug Modernization Act and various "guidance" documents issued pursuant to this legislation. Part II also describes some of the criminal and civil penalties that can be imposed for violating the FDA's restrictions on the marketing of off-label uses. Part III discusses potential liability under the Racketeer Influenced and Corrupt Organizations Act ("RICO"), with particular attention to two recent cases, *Hamm v. Rhone-Poulenc Rorer Pharmaceuticals, Inc.*<sup>18</sup> and *In re Neurontin Marketing, Sales Practices, and Products Liability Litigation*.<sup>19</sup> Part III will also discuss the liability of drug companies under the False Claims Act for directly and indirectly obtaining compensation from the federal government for the sale of products for off-label uses. Tort liability is the focus of Part IV. This includes tort claims based on violations of the Food, Drug and Cosmetic Act, fraudulent misrepresentation, failure to warn about the risks of particular off-label uses, and failure to test for risks associated with off-

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<sup>14</sup> Salbu, *supra* note 6, at 194.

<sup>15</sup> See, e.g., *Bristol-Meyers Squibb Co. v. Shalala*, 91 F.3d 1493, 1500 (D.C. Cir. 1996); *Ortho Pharm. Corp. v. Cosprophar, Inc.*, 32 F.3d 690, 692 (2d Cir. 1994); *Upjohn Co. v. MacMurdo*, 562 So. 2d 680, 683 (Fla. 1990).

<sup>16</sup> Beck & Azari, *supra* note 9, at 77.

<sup>17</sup> See *infra* at II.B.

<sup>18</sup> 187 F.3d 941 (8th Cir. 1999).

<sup>19</sup> 433 F. Supp. 2d 172 (D. Mass. 2006).

label uses. Finally, Part V evaluates the FDA's current policy concerning the promotion of off-label uses and concludes that it is too restrictive.

## II. FDA REGULATION OF PHARMACEUTICAL PRODUCTS

### A. *The FDA Drug Approval Process*

The Federal Food, Drug and Cosmetic Act ("FDCA")<sup>20</sup> authorizes the FDA to regulate the manufacture and marketing of prescription drugs and medical devices.<sup>21</sup> Under the FDCA, the FDA must license any "new drug" before it may be marketed.<sup>22</sup> The approval process begins with the submission of an Investigational New Drug Application.<sup>23</sup> If the application is approved, the sponsor may proceed with the New Drug Application ("NDA") process.<sup>24</sup> The first phase of this process usually involves animal testing to determine toxicity.<sup>25</sup> The drug then undergoes various types of clinical trials on human subjects.<sup>26</sup> When the clinical trials have been completed, the sponsor must submit an NDA to the FDA for review. The NDA must include a list of all of the drug's ingredients, detailed chemical information, detailed biological information, summaries of clinical testing results, a summary of the risks and

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<sup>20</sup> 21 U.S.C. §§ 301-399 (2000).

<sup>21</sup> See Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1764-835 (1996); see also Michael D. Green & William B. Schultz, *Tort Law Deference to FDA Regulation of Medical Devices*, 88 GEO. L.J. 2119, 2127-30 (2000) (discussing the difference between regulations for prescription drugs and medical devices). The FDA also regulates over-the-counter pharmaceutical products. See Kenneth C. Baumgartner, *A Historical Examination of the FDA's Review of the Safety and Effectiveness of Over-the-Counter Drugs*, 43 FOOD DRUG COSM. L.J. 463, 465-71 (1988).

<sup>22</sup> 21 U.S.C. § 355.

<sup>23</sup> See *id.* § 355(i); Center for Drug Evaluation and Research, Drug Applications, [http://www.fda.gov/cder/Regulatory/applications/ind\\_page\\_1.htm](http://www.fda.gov/cder/Regulatory/applications/ind_page_1.htm) (last visited Apr. 24, 2008).

<sup>24</sup> Note, *A Question of Competence: The Judicial Role in the Regulation of Pharmaceuticals*, 103 HARV. L. REV. 773, 776 (1990). A somewhat different process applies to the approval of medical devices. See Beck & Azari, *supra* note 9, at 72-75.

<sup>25</sup> James A. Wilsker, Note, *One-Half Phen in the Morning/One Fen Before Dinner: A Proposal for FDA Regulation of Off-Label Uses of Drugs*, 6 J.L. & POL'Y 795, 806 (1998).

<sup>26</sup> Richard A. Epstein, *Regulatory Paternalism in the Market for Drugs: Lessons from Vioxx and Celebrex*, 5 YALE J. HEALTH POL'Y L. & ETHICS 741, 756 (2005). Clinical trials are usually divided into Phase I, Phase II, and Phase III: Phase I trials determine whether a small number of test subjects can tolerate various levels of exposure to the drug; Phase II trials evaluate the safety and effectiveness of the drug on a larger group of persons for whom the drug is ultimately intended; and Phase III trials carry out additional tests to determine the drug's safety and efficacy. *Id.*

benefits of the drug, an environmental impact statement, marketing history, and proposed labeling.<sup>27</sup>

A drug may only be marketed and labeled for the uses for which it received approval from the FDA.<sup>28</sup> The FDA requires that a drug's label include information necessary for safe and effective use, warnings, precautions, clinical pharmacology, indications, contraindications, and information about adverse reactions.<sup>29</sup> FDA-approved labeling, which is primarily directed at physicians and other health care providers, is included as a product package insert and as an entry in the Physician's Desk Reference.<sup>30</sup> If a manufacturer wishes to add new approved uses to a drug's labeling, it must submit a new NDA to the FDA.<sup>31</sup>

The FDA's approval process for medical devices, on the other hand, is governed by the Medical Device Amendments ("MDA").<sup>32</sup> The MDA creates three classes of medical devices that receive different levels of regulation. Class I devices are merely subject to "general controls" by the FDA.<sup>33</sup> Class II devices are those for which "the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device."<sup>34</sup> Class III medical devices are those (1) for which there is insufficient information to determine that general controls and special controls are adequate to provide reasonable assurance of safety and effectiveness, and (2) are purported to be for sustaining human life or preventing impairment of human health, or present an unreasonable risk of illness or injury.<sup>35</sup>

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<sup>27</sup> 21 C.F.R. § 314.50 (2007); see also Beck & Azari, *supra* note 9, at 75-76.

<sup>28</sup> Beck & Azari, *supra* note 9, at 76.

<sup>29</sup> Salbu, *supra* note 6, at 186-87.

<sup>30</sup> Edmund Polubinski, III, Note, *Closing the Channels of Communication: A First Amendment Analysis of the FDA's Policy on Manufacturer Promotion of "Off-Label" Use*, 83 VA. L. REV. 991, 995 (1997).

<sup>31</sup> Kaspar J. Stoffelmayr, Comment, *Products Liability and "Off-Label" Uses of Prescription Drugs*, 63 U. CHI. L. REV. 275, 277 (1996).

<sup>32</sup> 21 U.S.C. §§ 351-360n (2000).

<sup>33</sup> Robert S. Adler & Richard A. Mann, *Preemption and Medical Devices: The Courts Run Amok*, 59 MO. L. REV. 895, 913 n.88 (1994). "General controls" under the MDA include such requirements as maintenance of good manufacturing practices, sanitary packaging, and accurate labeling. *Baker v. Smith & Nephew Richards, Inc.*, No. 95-58737, 1999 WL 811334, at \*5 n.14 (Tex. Dist. Ct. 1999). Class I devices include items such as surgeon's gloves, eye pads and ice bags. 21 C.F.R. § 880.6050 (2007).

<sup>34</sup> 21 U.S.C. § 360c(a)(1)(B). Class II devices include items such as tampons, syringes, and neonatal incubators. 21 C.F.R. §§ 884.5460, 880.5860, 880.5400 (2007).

<sup>35</sup> 21 U.S.C. § 360c(a)(1)(C). Pacemakers and heart valves are examples of Class III devices. 21 C.F.R. §§ 870.3610, 870.3925 (2007).

Ordinarily, the manufacturer of a Class III medical device must submit a premarket approval application (“PMA”) to the FDA before marketing the device in interstate commerce.<sup>36</sup> The PMA must contain a full report of any clinical investigations that concern the safety or effectiveness of the device.<sup>37</sup> It must also contain “a full statement of the components, ingredients, and properties and of the . . . principles of operation, of such device.”<sup>38</sup> In addition, it must include “a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, the device.”<sup>39</sup> In the PMA, the applicant must identify, discuss, and analyze

any other data, information, or report relevant to an evaluation of the safety and effectiveness of the device known to or that should reasonably be known to the applicant from any source, foreign or domestic, including information derived from investigations other than those proposed in the application and from commercial marketing experience.<sup>40</sup>

The PMA must also include specimens of the labeling proposed to be used for the device.<sup>41</sup> A Class III medical device is not subject to the PMA requirement if (1) it was marketed prior to the MDA’s enactment<sup>42</sup> and a regulation requiring submission of PMAs has not been issued for the device or (2) it is “substantially equivalent” to a predicate device, that is, one marketed prior to the MDA’s enactment.<sup>43</sup> Another exception to the PMA process permits a Class III device that obtains an Investigational Device Exemption (“IDE”) to be tested on human subjects without obtaining PMA approval.<sup>44</sup>

Thus, manufacturers of both prescription drugs and medical devices must satisfy the FDA that their products are safe and effective before the agency will approve them for marketing.

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<sup>36</sup> 21 U.S.C. § 360e.

<sup>37</sup> *Id.* § 360e(c)(1)(A); 21 C.F.R. § 814.20(b)(8)(i) (2007).

<sup>38</sup> 21 U.S.C. § 360e(c)(1)(B).

<sup>39</sup> *Id.* § 360e(c)(1)(C).

<sup>40</sup> 21 C.F.R. § 814.20(b)(8)(ii) (2007).

<sup>41</sup> 21 U.S.C. § 360e(c)(1)(F).

<sup>42</sup> *Id.* § 360e(b)(1)(A).

<sup>43</sup> *Id.* § 360e(b)(1)(B).

<sup>44</sup> *See id.* § 360j(g). An IDE allows researchers to conduct clinical trials without first going through a formal PMA process in order to “encourage . . . the discovery and development of useful devices . . . and maintain optimum freedom for scientific investigators.” 21 U.S.C. § 360j(g).

B. *FDA Regulation of the Promotion of Off-Label Uses by Drug Manufacturers*

Although the FDCA authorizes the FDA to regulate the manufacture and marketing of prescription drugs and medical devices, the FDA has never claimed any authority to regulate the practice of medicine.<sup>45</sup> Therefore, physicians may use FDA-licensed drugs or medical devices in any way they believe will benefit their patients and are not limited to approved uses.<sup>46</sup> However, the FDA can regulate advertising and promotion activities by drug manufacturers. In the past, the FDA prohibited manufacturers from promoting a drug for any purpose that had not been approved.<sup>47</sup> A company that promoted information about uses that had not received FDA approval was subject to liability for "misbranding."<sup>48</sup> The only exception to this policy was for the provision of information about off-label uses when specifically requested by a physician.<sup>49</sup> There were two reasons for the FDA's prohibition of the dissemination of information about off-label uses. First, the FDA was concerned that the information about off-label uses provided by pharmaceutical companies to doctors might be incomplete.<sup>50</sup> Second, the FDA believed that allowing drug manufacturers to furnish such information would encourage them to bypass the FDA's NDA process.<sup>51</sup>

Eventually, the FDA issued guidance documents that permitted the dissemination of information about off-label uses in published form and at independent medical education programs. The first of these guidance documents sought to control drug manufacturers' distribution of "enduring materials," such as textbooks and reprints of journal articles.<sup>52</sup> In 1997, Congress enacted the Food and Drug Administration Modernization Act ("FDAMA"),<sup>53</sup> and Section 401 of the Act

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<sup>45</sup> Polubinski, *supra* note 30, at 999.

<sup>46</sup> Beck & Azari, *supra* note 9, at 76.

<sup>47</sup> Wilsker, *supra* note 25, at 808.

<sup>48</sup> James O'Reilly & Amy Dalal, *Off-Label or Out of Bounds? Prescriber and Marketer Liability for Unapproved Uses of FDA-Approved Drugs*, 12 ANNALS HEALTH L. 295, 301 (2003).

<sup>49</sup> Greene, *supra* note 5, at 49.

<sup>50</sup> Weeks, *supra* note 8, at 657.

<sup>51</sup> Greene, *supra* note 5, at 48-49.

<sup>52</sup> Advertising and Promotion; Guidances, 61 Fed. Reg. 52,800-52,801 (Oct. 8, 1996); *see also infra* text accompanying notes 56-58.

<sup>53</sup> Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 401, 111 Stat. 2296, 2356 (1997) (codified at 21 U.S.C. § 355 et seq. (2000)).

incorporated the guidance provisions.<sup>54</sup> According to FDAMA, a manufacturer was allowed to provide health care practitioners, pharmacy benefit managers, health insurance companies, group health plans, or governmental agencies with information about the safety, effectiveness, or benefits of an off-label use, provided that the manufacturer filed a supplemental application for the proposed off-label use with the FDA.<sup>55</sup> In addition, the information disseminated to these qualified groups had to be in the form of unabridged peer-reviewed articles or qualified reference publications.<sup>56</sup> Furthermore, the manufacturer was required to disclose that the use in question had not been approved or cleared by the FDA.<sup>57</sup>

In 1997, the FDA also published the "Final Guidance on Industry-Supported Scientific and Educational Activities"<sup>58</sup> to regulate continuing medical education ("CME") programs at which information about off-label uses was presented.<sup>59</sup> The CME Guidance gave FDA approval to CME programs in which discussion of off-label uses was not influenced by pharmaceutical companies, but disapproved programs in which off-label uses were discussed when the programs were controlled or influenced by drug manufacturers.<sup>60</sup> To that end, the CME Guidance identified a number of factors to be considered in determining whether a program was independent of manufacturer influence and, therefore, permissible.<sup>61</sup>

As mentioned above, Section 401 of the FDAMA allowed drug companies to disseminate information about off-label uses of FDA-approved products, but it expired on September 30,

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<sup>54</sup> *Id.*; see 21 U.S.C. § 360aaa to 360aaa-6(a) (2000).

<sup>55</sup> 21 U.S.C. § 360aaa(a).

<sup>56</sup> *Id.* § 360aaa-1(a).

<sup>57</sup> *Id.* §360aaa(b)(6)(A)(i).

<sup>58</sup> 62 Fed. Reg. 64,074 (Dec. 3, 1997).

<sup>59</sup> I. Scott Bass et al., *Off-Label Promotion: Is FDA's Final Guidance on Industry-Supported Scientific and Educational Programs Enforceable?*, 53 FOOD & DRUG L.J. 193, 195 (1998).

<sup>60</sup> Greene, *supra* note 5, at 49.

<sup>61</sup> Final Guidance on Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64,074, 64,097-99 (Dec. 3, 1997). These factors include (1) who controls the content and selects the moderator and speakers; (2) whether drug manufacturer funding is disclosed; (3) whether unapproved uses will be discussed; (4) whether the central focus of the program is on one product; (5) the relationship between the corporate sponsors and the CME provider; (6) the process by which the audience is selected; (7) the availability of opportunities for meaningful discussion and questioning; (8) the dissemination of information; (9) the existence of ancillary promotional activities; and (10) complaints by the provider, participants or attendees about attempts by the supporting company to influence the program's content. *Id.*

2006.<sup>62</sup> Filling the regulatory void left by the FDAMA's expiration, the FDA promulgated on February 15, 2008 a draft guidance document entitled "Good Reprint Practices," which identifies how drug manufacturers should distribute scientific or medical journal reprints, articles, or reference works.<sup>63</sup> This draft guidance document provides that the article or reference work recommending an off-label use should be published by an organization that has an editorial board.<sup>64</sup> In addition, the publisher should fully disclose conflicts of interest or biases on the part of any author, contributor, or editor associated with an article.<sup>65</sup> Articles should also be peer reviewed and published in accordance with established procedures.<sup>66</sup> Furthermore, the draft guidance document discourages the distribution of special supplements or publications that have been funded by the manufacturer whose product is discussed in an article.<sup>67</sup> Moreover, it provides that the FDA considers articles that are not supported by credible medical evidence to be false and misleading and prohibits manufacturers from distributing them.<sup>68</sup> The draft guidance document also requires that the reprint or reference publication be distributed in unabridged form.<sup>69</sup> Finally, the draft guidance document makes it clear that the FDA retains its power to determine whether distribution of an article or publication constitutes promotion of an unapproved "new use" or whether such a product may be considered misbranded or adulterated under the Federal Food, Drug and Cosmetic Act.<sup>70</sup>

The new FDA policy on the promotion of off-label uses, beginning with the passage of the FDAMA, is less restrictive than its previous approach, which prohibited manufacturers from providing *any* information about off-label uses unless physicians specifically asked for it. However, commentators

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<sup>62</sup> *Id.*; see *supra* notes 54-57 and accompanying text (discussing Section 401).

<sup>63</sup> 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 (2008), *available at* <http://www.fda.gov/oc/op/goodreprint.html>.

<sup>64</sup> *Id.* pt. IV.A.

<sup>65</sup> *Id.*

<sup>66</sup> *Id.*

<sup>67</sup> *Id.*

<sup>68</sup> *Id.*

<sup>69</sup> *Id.* pt. IV.B.

<sup>70</sup> *Id.* pt. III.

have been critical of the guidance documents,<sup>71</sup> and it appears that drug companies have shown little enthusiasm for working within the structure set forth by the FDA in these documents.

### C. *Violations of FDA Regulations*

A drug company that improperly promotes its products for off-label uses will be subject to criminal sanctions and civil liability.<sup>72</sup> The FDA considers unauthorized promotion to be misbranding.<sup>73</sup>

The recent experience of Purdue Pharma, manufacturer of the prescription pain medication OxyContin, illustrates the perils of misbranding and other violations of the FDCA. The company was accused of encouraging physicians to prescribe OxyContin for use every eight hours instead of the twelve-hour dosage approved by the FDA.<sup>74</sup> It eventually agreed to pay \$19.5 million to twenty-six states and the District of Columbia to settle a civil suit based on its alleged promotion of off-label use of the painkiller.<sup>75</sup> This led Connecticut Attorney General Richard Blumenthal to declare, “We are raising the bar on off-label marketing—and other promotion tactics—that lead to abuse and diversion of prescription drugs.”<sup>76</sup> However, Purdue Pharma suffered an even more serious blow when the U.S. Department of Justice brought criminal charges against the company and three of its top executives.<sup>77</sup> Federal prosecutors contended that Purdue Pharma had engaged in a fraudulent and deceptive marketing campaign that falsely claimed that

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<sup>71</sup> *E.g.*, Bass et al., *supra* note 59, at 209-12; Salbu, *supra* note 6, at 220-21; Polubinski, *supra* note 30, at 993, 1031.

<sup>72</sup> Violations of the FDCA can result in fines, imprisonment, and civil penalties. 21 U.S.C. § 333 (2006).

<sup>73</sup> Mark A. Ford, Note, *Another Use of OxyContin: The Case for Enhancing Liability for Off-Label Drug Marketing*, 83 B.U. L. REV. 429, 438-39 (2003). The Food, Drug and Cosmetic Act generally considers a drug “misbranded” if its labeling fails to contain “adequate directions for use.” 21 U.S.C. § 352(f) (2000). When the FDA approves a prescription drug or medical device for marketing, it approves specific labeling for the product. If a manufacturer promotes a drug for an unapproved use, its FDA-approved labeling will not contain any directions for that use and thus will be misbranded under § 352(f). Ford, *supra*, at 438.

<sup>74</sup> *Painkiller’s Maker Settles Complaint*, N.Y. TIMES, May 9, 2007, at C6.

<sup>75</sup> *Id.*

<sup>76</sup> Press Release, Richard Blumenthal, Attorney General, & Jerry Farrell, Jr., Attorney General, [Department of Consumer Protection] Commissioner [Conn.] Announce Oxycontin Maker Agrees to Halt Illegal Marketing 1 (May 8, 2007), available at [http://www.ct.gov/dcp/lib/dcp/pdf/oxycontin\\_multistate\\_settlement.pdf](http://www.ct.gov/dcp/lib/dcp/pdf/oxycontin_multistate_settlement.pdf).

<sup>77</sup> Barry Meier, *Narcotic Maker Guilty of Deceit Over Marketing*, N.Y. TIMES, May 11, 2007, at A1.

OxyContin, because of its timed-release formula, was more resistant to abuse and less likely to cause addiction than competing products such as Percocet.<sup>78</sup> The federal government also charged some company sales representatives with giving doctors misleading scientific data to support their fraudulent claims.<sup>79</sup>

Pursuant to an agreement, Purdue Pharma and the three corporate officers pleaded guilty to these criminal charges.<sup>80</sup> As part of the plea bargain deal, Purdue Pharma acknowledged that it had made false statements, and it agreed to pay \$470 million in fines and payments to various state and federal agencies as well as \$130 million to settle civil lawsuits brought against the company by former patients who claimed to have become addicted to OxyContin.<sup>81</sup> According to federal prosecutors, the \$600 million in fines and civil penalties that Purdue Pharma agreed to pay amounted to ninety percent of the profits that it initially made from OxyContin sales.<sup>82</sup> Furthermore, as part of the plea bargain deal, the court sentenced the company to five years' probation.<sup>83</sup>

Three company executives also pleaded guilty to misdemeanor charges of misbranding OxyContin, a violation of the FDCA that does not require proof that the defendants intended to defraud doctors or consumers or that they knew about the wrongdoing of others.<sup>84</sup> These officials agreed to pay a total of \$34.5 million in fines.<sup>85</sup> At a "lengthy and highly emotional hearing" in federal district court, parents of those who had died from overdoses of OxyContin condemned the company officials and urged the court to reject the plea agreements and sentence the officials to jail terms.<sup>86</sup> However, the court accepted the plea agreements and only sentenced the three officials to three years' probation and 400 hours each of community service in drug treatment programs.<sup>87</sup> Nevertheless,

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<sup>78</sup> *Id.*

<sup>79</sup> *Id.*

<sup>80</sup> *Id.*

<sup>81</sup> *Id.*

<sup>82</sup> Barry Meier, *Big Part of OxyContin Profit Was Consumed by Penalties*, N.Y. TIMES, June 19, 2007, at C3.

<sup>83</sup> Barry Meier, *3 Officials Sentenced in Case Involving OxyContin*, N.Y. TIMES, July 21, 2007, at C4.

<sup>84</sup> *Id.*

<sup>85</sup> Meier, *supra* note 82.

<sup>86</sup> Meier, *supra* note 83.

<sup>87</sup> *Id.*

the judge expressed disappointment that he was unable to send the defendants to prison because federal prosecutors had not produced evidence that the company officials were aware of the wrongdoing at Purdue Pharma.

*Purdue Pharma* illustrates that pharmaceutical companies and their executive officers who violate FDA regulations by promoting off-label uses run the risk of incurring huge fines or even incarceration if they are caught.

### III. LIABILITY BASED ON VIOLATIONS OF THE RACKETEER INFLUENCED AND CORRUPT ORGANIZATIONS ACT AND THE FALSE CLAIMS ACT

Two other sources of statutory liability for manufacturers that promote off-label uses for their products are the Racketeer Influenced and Corrupt Organizations Act (“RICO”) and the False Claims Act.

#### A. RICO

A number of RICO cases have been brought against pharmaceutical companies for illegally promoting off-label uses of prescription drugs. Although drug companies have won several of these cases, others are still in litigation.

##### 1. Elements of RICO

RICO was enacted in 1970 to combat the infiltration of organized crime into legitimate business enterprises.<sup>88</sup> The statute imposes criminal and civil liability on any person who invests income from a pattern of racketeering activity in an enterprise,<sup>89</sup> acquires an interest in an enterprise through a pattern of racketeering activity,<sup>90</sup> conducts an enterprise’s affairs through a pattern of racketeering activity,<sup>91</sup> or who conspires to do any of these things.<sup>92</sup> An “enterprise” includes “any individual, partnership, corporation, association, or other

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<sup>88</sup> Beth S. Schipper, Note, *Civil RICO and Parens Patriae: Lowering Litigation Barriers Through State Intervention*, 24 WM. & MARY L. REV. 429, 431 (1983); see also Bryce A. Jensen, Note, *From Tobacco to Health Care and Beyond—A Critique of Lawsuits Targeting Unpopular Industries*, 86 CORNELL L. REV. 1334, 1354 (2001).

<sup>89</sup> 18 U.S.C. § 1962(a) (2000).

<sup>90</sup> *Id.* § 1962(b).

<sup>91</sup> *Id.* § 1962(c).

<sup>92</sup> *Id.* § 1962(d).

legal entity, and any union or group of individuals associated in fact although not a legal entity."<sup>93</sup> RICO defines "racketeering activity" to include various criminal acts such as mail fraud, wire fraud, drug trafficking, murder, arson, gambling, extortion, bribery, and embezzlement.<sup>94</sup> According to the statute, a "pattern of racketeering activity" consists of two or more acts of racketeering that occur within ten years of each other and that reflect a relationship and continuity in terms of purpose, results, participants, victims, or methods, but which are sufficiently distinct so that they amount to more than a single episode or an isolated occurrence.<sup>95</sup> Because at least two of these offenses must be committed in order to make out a claim under RICO, they are referred to as "predicate acts."<sup>96</sup>

There are two types of civil remedies available under RICO: damages and equitable relief. Any person injured in his business or property by reason of a RICO violation may sue for treble damages.<sup>97</sup> In addition, a court may grant various equitable remedies, including restricting the defendants from engaging in certain activities in the future and even dissolving or restructuring the enterprise.<sup>98</sup> Furthermore, RICO expressly authorizes the U.S. Attorney General to seek equitable relief in appropriate cases.<sup>99</sup>

## 2. *Hamm v. Rhone-Poulenc Rorer Pharmaceuticals, Inc.*

*Hamm v. Rhone-Poulenc Rorer Pharmaceuticals, Inc.* ("RPR") illustrates the application of RICO in the context of off-label drug use promotion.<sup>100</sup> The case involved the drugs Lovenox, Taxotere, Rilutek, and Nasacort AQ.<sup>101</sup> An RPR employee and three former employees brought a civil claim

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<sup>93</sup> *Id.* § 1961(4).

<sup>94</sup> *Id.* § 1961(1).

<sup>95</sup> *Id.* § 1961(5).

<sup>96</sup> Ed Dawson, Note, *Legigation*, 79 TEX. L. REV. 1727, 1740 (2001).

<sup>97</sup> 18 U.S.C. § 1964(c).

<sup>98</sup> *Id.* § 1964(a).

<sup>99</sup> *Id.* § 1964(b).

<sup>100</sup> See *Hamm v. Rhone-Poulenc Rorer Pharm., Inc.*, 187 F.3d 941 (8th Cir. 1999).

<sup>101</sup> *Id.* at 946 (8th Cir. 1999). Lovenox was approved for use as a treatment for blood clotting; Taxotere was approved for cancer therapy; Rilutek was approved for amyotrophic lateral sclerosis ("ALS," also known as Lou Gehrig's disease); and Nasacort was approved to treat asthma. See Respondent's Brief in Opposition for Respondent Rhone-Poulenc Rorer Pharmaceuticals Inc. at 4, *Hamm v. Rhone-Poulenc Rorer Pharm., Inc.*, 528 U.S. 1117 (2000) (No. 99-803), available at 1999 WL 33632777.

under RICO against RPR; Genecom, RPR's advertising agency; and a number of physicians who allegedly received illegal payments from RPR. The plaintiffs claimed that RPR illegally marketed drugs for off-label uses by providing information about off-label uses to its sales representatives and encouraging them to solicit physicians to prescribe its products for such uses.<sup>102</sup> In addition, according to the plaintiffs, RPR, through Genecom, engaged physicians who prescribed RPR products for off-label uses to speak at CME events and paid them to promote off-label uses.<sup>103</sup> The plaintiffs also alleged that RPR set sales quotas for its staff that implicitly included off-label sales and that when the plaintiffs reported these unlawful promotional activities to RPR lawyers, they were told to rewrite promotional event payment documents and destroy other evidence of illegal promotions.<sup>104</sup>

Furthermore, the plaintiffs alleged that RPR and other defendants also violated RICO by conducting or participating in a pattern of racketeering activity by obtaining money from product sales generated by the illegal promotion of off-label uses of its products.<sup>105</sup> The plaintiffs declared that RPR and other defendants sent promotional materials and obtained or paid money through the mail, transmitted promotional materials and made false representations through the use of interstate telephonic communications, and used the facilities of interstate commerce to distribute the proceeds gained from illegal kickbacks and payments made to influence the promotion and use of RPR products.<sup>106</sup>

Notwithstanding these allegations of wrongdoing, the lower court dismissed the plaintiffs' civil RICO claims for lack of standing,<sup>107</sup> and this decision was affirmed on appeal.<sup>108</sup> The court declared that RICO's civil enforcement provisions required that a plaintiff be "injured in his [or her] business or property by reason of a violation of section 1962."<sup>109</sup> Therefore, in order to have standing to sue under RICO, a plaintiff must allege (1) an injury to "business or property" (2) caused "by

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<sup>102</sup> *Hamm*, 187 F.3d at 946.

<sup>103</sup> *Id.*

<sup>104</sup> *Id.*

<sup>105</sup> *Id.*

<sup>106</sup> *Id.*

<sup>107</sup> *Hamm v. Rhone-Poulenc Rorer Pharm., Inc.*, 176 F.R.D. 566, 571 (D. Minn. 1997).

<sup>108</sup> *Hamm*, 187 F.3d at 954.

<sup>109</sup> *Id.* at 951 (quoting 18 U.S.C. § 1964(c)).

reason of" a RICO violation.<sup>110</sup> The court pointed out that the U.S. Supreme Court held in *Sedima, S.P.R.L. v. Imrex Co.*<sup>111</sup> that plaintiffs must be injured by conduct that constitutes racketeering activity (that is, predicate acts) and not by other wrongful acts committed by the defendant to have standing to sue under RICO.<sup>112</sup> This requirement is imposed because the compensable harm under RICO is the commission of predicate acts in connection with the conduct of an enterprise.<sup>113</sup> In this case, however, the defendants' fraudulent scheme to promote off-label uses of its products had not been directed at the plaintiffs, but at hospital administrators, physicians, and other medical personnel who prescribed and purchased RPR's pharmaceutical products.<sup>114</sup> The court concluded that since the employees had not been the intended targets of the alleged racketeering activity, they did not have standing to bring a civil RICO suit.<sup>115</sup>

Although the plaintiffs were not directly injured by RPR's illegal promotion of off-label uses of its products, they argued that they suffered the requisite injury to business or property by alleging that they had been terminated, denied promotions or raises, and defamed, as well as had lost stock options, after having criticized or refused to participate in RPR's off-label promotion scheme.<sup>116</sup> In response, the court pointed out that it had rejected similar allegations in *Bowman v. Western Auto Supply Co.*<sup>117</sup> as a viable basis for a civil RICO lawsuit.<sup>118</sup> According to the court in *Bowman*, "The simple act of discharging an employee . . . does not constitute racketeering activity as defined in RICO, and thus does not fall within the definition of what the Supreme Court has termed 'predicate acts' under RICO."<sup>119</sup> The plaintiffs argued that *Bowman* did not bar their RICO claims for defamation or damage to their business reputations.<sup>120</sup> The court, however, declared that the plaintiffs could only sue under RICO if their injuries were

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<sup>110</sup> *Id.*

<sup>111</sup> 473 U.S. 479, 496-97 (1985).

<sup>112</sup> *Hamm*, 187 F.3d at 952.

<sup>113</sup> *Id.* (quoting *Sedima*, 473 U.S. at 497).

<sup>114</sup> *Id.*

<sup>115</sup> *Id.*

<sup>116</sup> *Id.* at 947.

<sup>117</sup> 985 F.2d 383, 385-86 (8th Cir. 1993).

<sup>118</sup> *Hamm*, 187 F.3d at 952.

<sup>119</sup> *Bowman*, 985 F.2d at 385-86.

<sup>120</sup> *Hamm*, 187 F.3d at 953.

*directly* caused by RICO violations.<sup>121</sup> In this case, since the plaintiffs were not the targets of the fraudulent scheme, any damage to the plaintiffs' business reputations was too indirect and remotely related to the defendant's racketeering activities to support their RICO claim.<sup>122</sup>

The court also concluded that the plaintiffs lacked standing because they failed to show any injury to their "business or property" as required by section 1964(c) of the RICO statute.<sup>123</sup> The court observed that damage to one's business reputation is a personal injury and not an injury to business or property.<sup>124</sup> Finally, the court rejected the plaintiffs' argument that they could bring a conspiracy claim under RICO as long as their injuries were caused by an overt act in furtherance of the conspiracy, even though the act in question was not a predicate act.<sup>125</sup> Although the court acknowledged that there was a circuit split on this issue, it decided to treat conspiracy the same as other claims for which a predicate act was required, as the *Bowman* court had done, because "[i]mposing the predicate act requirement on civil claims based on violations of § 1962(d) narrows the focus of those suits to the specific racketeering activity that lies at the heart of the RICO statute."<sup>126</sup>

*Hamm v. Rhone-Poulenc Rorer* illustrates some of the difficulties plaintiffs face in civil RICO cases. However, as the *Neurontin* case discussed below shows, RICO may still be a potential source of liability for drug companies that illegally promote off-label uses.

### 3. *In re Neurontin Marketing, Sales Practices, and Products Liability Litigation*

*In re Neurontin Marketing* serves as another example of how RICO claims may be brought against pharmaceutical

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<sup>121</sup> *Id.* (citing *Holmes v. Sec. Investor Prot. Corp.*, 503 U.S. 258, 269-70 (1992)).

<sup>122</sup> *Id.* at 954.

<sup>123</sup> *Id.*

<sup>124</sup> *Id.* (citing *Chicago Heights v. Lobue*, 914 F. Supp. 279, 285 (N.D. Ill. 1996); *In re Teledyne Def. Contracting Derivative Litig.*, 849 F. Supp. 1369, 1372 n.1 (C.D. Cal. 1993)).

<sup>125</sup> *Id.*

<sup>126</sup> *Id.* (quoting *Bowman*, 985 F.2d at 388).

companies for promoting off-label uses.<sup>127</sup> The case involved a class action by medical insurers against Pfizer and Warner-Lambert Co., alleging that the pharmaceutical companies had engaged in a "fraudulent scheme to market the prescription drug Neurontin for a variety of off-label uses."<sup>128</sup> The defendants moved to dismiss both the Amended Class Complaint and the First Coordinated Amended Complaint.<sup>129</sup> A magistrate judge recommended that the motion be granted in part and denied in part.<sup>130</sup> After a hearing, the district court endorsed most of the magistrate's report, holding that the plaintiffs adequately alleged the existence of an enterprise and a pattern of racketeering activity.<sup>131</sup> In addition, the court concluded that the plaintiffs had sufficiently alleged the existence of a conspiracy.<sup>132</sup>

The court's opinion primarily focused on whether the plaintiffs adequately alleged the existence of an "enterprise" and whether the defendants had engaged in a "pattern of racketeering activity." The court noted that the existence of an enterprise and the pattern of racketeering activity engaged in by the enterprise are separate and distinct elements of a RICO claim.<sup>133</sup> However, according to the court, "proof of these two elements need not be separate or distinct but may in fact 'coalesce.'"<sup>134</sup>

With regard to the enterprise element, the court observed that according to the RICO statute, an enterprise includes "any individual, partnership, corporation, association, or other legal entity, and any union or group of individuals associated in fact although not a legal entity."<sup>135</sup> Although the Supreme Court has declared that this language should be

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<sup>127</sup> See *In re Neurontin Mktg., Sales Practices, & Prods. Liab. Litig.*, 433 F. Supp. 2d 172 (D. Mass. 2006).

<sup>128</sup> *Id.* at 176. In 1994, the FDA approved Neurontin for use as an adjunctive treatment for epilepsy. However, about half of Neurontin prescriptions were for off-label uses such as pain control and mono-therapy for epilepsy as well as treatment for bipolar conditions and attention deficit disorder. *United States ex rel. Franklin v. Parke-Davis, Div. of Warner-Lambert Co.*, 147 F. Supp. 2d 39, 45 (D. Mass. 2001).

<sup>129</sup> *In re Neurontin*, 433 F. Supp. 2d at 176-77.

<sup>130</sup> *Id.*

<sup>131</sup> *Id.* at 178-84.

<sup>132</sup> *Id.* at 184.

<sup>133</sup> *Id.* at 178.

<sup>134</sup> *Id.* (citing *United States v. Patrick*, 248 F.3d 11, 19 (1st Cir. 2001)).

<sup>135</sup> *Id.* at 177 (quoting 18 U.S.C. § 1961(4)).

interpreted broadly,<sup>136</sup> an enterprise is limited to “a group of persons associated together for a common purpose of engaging in a course of conduct.”<sup>137</sup>

In the *Neurontin* case, the plaintiffs alleged that the defendants had created a large association-in-fact type of enterprise, composed of numerous marketing firms and physicians, in order to illegally promote off-label uses of Neurontin.<sup>138</sup> As an alternative theory, the plaintiffs claimed that the defendants had created two smaller enterprises: one that carried out peer-to-peer selling of Neurontin for off-label uses and one that produced ghost-written articles promoting off-label uses of the drug.<sup>139</sup> In addition to these theories, the plaintiffs also contended that the defendants had created enterprises with various medical marketing firms, with or without physicians who promoted Neurontin.<sup>140</sup> To support these claims, the plaintiffs alleged that the defendants had joined together with marketing firms both to host events designed to promote Neurontin and also to publish articles that proclaimed the drug’s effectiveness for various off-label uses.<sup>141</sup> According to the plaintiffs, the defendants and their medical marketing partners had organized events designed to tout Neurontin while giving the appearance of being independent, and physicians had been paid by the defendants or their medical marketing firms to speak at these events and describe the favorable results they had obtained from off-label uses of Neurontin.<sup>142</sup> Lastly, the plaintiffs alleged that the defendants had selected material from the medical literature about off-label uses of Neurontin, had sent it to medical marketing firms who would then write articles based on this material, and then had paid physicians to take credit as authors of the pieces when they were published.<sup>143</sup>

In considering whether the plaintiffs established the existence of an enterprise, the court first observed that an enterprise must have a *common purpose* to satisfy the enterprise requirement. According to the plaintiffs, the common

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<sup>136</sup> *Sedima, S.P.R.L. v. Imrex Co., Inc.*, 473 U.S. 479, 497-98 (1985); *United States v. Turkette*, 452 U.S. 576, 586-87 (1981).

<sup>137</sup> *Turkette*, 452 U.S. at 583.

<sup>138</sup> *In re Neurontin*, 433 F. Supp. 2d at 178.

<sup>139</sup> *Id.*

<sup>140</sup> *Id.*

<sup>141</sup> *Id.*

<sup>142</sup> *Id.*

<sup>143</sup> *Id.*

purpose of each of the alleged enterprises was to market Neurontin for off-label uses in violation of FDA regulations.<sup>144</sup> The magistrate's report conceded that members of the alleged enterprises may have shared a common purpose—to promote off-label uses of Neurontin—but noted that they did not share a common purpose to commit mail and wire fraud, the predicate acts alleged by the plaintiffs to support the RICO claim.<sup>145</sup> After observing that "[t]here has been considerable confusion as to whether the common purpose needs to be illegal," the court declared that the complaints adequately alleged an unlawful common purpose for each of the enterprises, "namely to illegally promote off-label uses of Neurontin."<sup>146</sup> However, as the court acknowledged, violation of FDA regulations was not "actionable" because violations of FDA regulations do not give rise to a private tort claim against the violator.<sup>147</sup>

The court distinguished *In re Pharmaceutical Industry Average Wholesale Price Litigation*, a case where the plaintiffs tried to establish the existence of an enterprise composed of drug manufacturers and publishers of prescription drug price compendiums.<sup>148</sup> In that case, the plaintiffs contended there was a common purpose between the manufacturers that had fraudulently inflated the average wholesale prices of drugs and the publishers of prescription drug compendia listing those inflated prices.<sup>149</sup> However, the court held that the plaintiffs failed to satisfy the enterprise requirement under RICO because the publishers had been indifferent to the success of the drug companies' fraudulent scheme and had had no intent themselves to defraud the medical community or the federal government when they published the price information.<sup>150</sup> In contrast, the plaintiffs in *Neurontin* alleged that the members of the enterprise joined together to engage in unlawful conduct to achieve a shared goal, thereby satisfying the common purpose element of the pleading.<sup>151</sup>

In the *Neurontin* court's discussion of the enterprise requirement, it observed that it was not enough for the

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<sup>144</sup> *Id.*

<sup>145</sup> *Id.* at 178-79.

<sup>146</sup> *Id.* at 179-80.

<sup>147</sup> *Id.*; see *infra* Part IV.A.1.

<sup>148</sup> *Id.*; see *In re Pharm. Indus. Average Wholesale Price Litig.*, 307 F. Supp. 2d 196, 201-03 (D. Mass. 2004).

<sup>149</sup> *In re Neurontin*, 433 F. Supp. 2d at 180.

<sup>150</sup> *Id.*

<sup>151</sup> *Id.* at 180-81.

plaintiffs to demonstrate that the parties had a common goal or purpose; they must also prove that the alleged enterprise was “an ongoing organization, not a set of smaller ad-hoc conspiracies engaged in the same activities independent of one another.”<sup>152</sup> The magistrate’s report found that the drug manufacturers, medical marketing firms, and physicians did not work together as part a cohesive group, but instead resembled a “hub-and-spoke” assemblage of a conspiracy.<sup>153</sup> The court examined the various enterprises identified by the plaintiffs to determine if any of them could be characterized as ongoing organizations functioning as continuing units and concluded that the relationship between the manufacturers of Neurontin and various marketing firms constituted an ongoing organization and not merely a series of ad hoc activities.<sup>154</sup>

In making this determination, the court first examined the alleged “global enterprise,” consisting of the defendant drug companies, all of the medical marketing firms, and all of the physicians who made presentations or wrote articles advocating off-label uses of Neurontin.<sup>155</sup> The court agreed with the magistrate’s report that neither the medical marketing firms nor the physicians worked together with the defendants as a cohesive unit; rather, they had formed a hub-and-spoke operation, with the drug companies at the center managing several independent relationships.<sup>156</sup> According to the court, the medical marketing firms and the physicians did not constitute an enterprise for purposes of RICO because there had been no “rim” to connect all of the spokes of the wheel.<sup>157</sup> In other words, the drug companies had communicated with individual medical marketing firms and physicians, but individual medical marketing firms and physicians had not communicated with one another.<sup>158</sup> Since the plaintiffs could not show that there was a network involving all of these drug companies, medical

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<sup>152</sup> *Id.* at 182.

<sup>153</sup> *Id.*

<sup>154</sup> *Id.*

<sup>155</sup> *Id.*

<sup>156</sup> *Id.*

<sup>157</sup> *Id.*

<sup>158</sup> *Id.*; see also *VanDenBroeck CommonPoint Mortgage Co.*, 210 F.3d 696, 700 (6th Cir. 2000); *In re Lupron Mktg. & Sales Practices Litig.*, 295 F. Supp. 2d 148, 174 n.29 (D. Mass. 2003); *First Nationwide Bank v. Gelt Funding Corp.*, 820 F. Supp. 89, 98 (S.D.N.Y. 1993).

marketing firms, and physicians, the court rejected their claim that a global enterprise existed.<sup>159</sup>

Next, the court considered whether the alleged various "sub-entities" devoted to peer-to-peer selling of Neurontin and publication of articles touting off-label uses of the drug qualified as enterprises for purposes of RICO.<sup>160</sup> The court concluded that these sub-entities had been composed of the same parties as the global enterprise and that, once again, the plaintiffs neither alleged the existence of a general agreement among these parties to carry out a common purpose nor alleged that there had been a cohesive network among these parties to accomplish common goals.<sup>161</sup> The court determined consequently that the sub-entity theory suffered from the same deficiency as the global enterprise allegation under RICO.<sup>162</sup>

Finally, the court evaluated the plaintiffs' claim that a series of smaller enterprises had existed, each comprised of the drug manufacturers and one of the physicians or marketing firms, effectively making each hub-and-spoke association a separate enterprise for purposes of RICO.<sup>163</sup> The court concluded that the plaintiffs sufficiently alleged that all the members of these purported enterprises had shared a common illegal purpose of promoting off-label uses of Neurontin.<sup>164</sup> The remaining question, therefore, was whether these smaller associations had been ongoing organizations or merely ad hoc criminal conspiracies.<sup>165</sup> In the case of associations between the defendant drug companies and medical marketing firms, the plaintiffs alleged that the defendants had formulated "tactical plans" with various marketing firms to promote off-label uses of Neurontin on an ongoing basis and that there had been regular communication between the defendants and these firms.<sup>166</sup> In addition, there had been financial ties between the parties as the defendants had transferred money to medical marketing firms to pay physicians to make presentations and claim authorship of articles endorsing off-label uses of the defendants' product.<sup>167</sup> In light of these allegations, the court

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<sup>159</sup> *In re Neurontin*, 433 F. Supp. 2d at 182.

<sup>160</sup> *Id.*

<sup>161</sup> *Id.* at 183.

<sup>162</sup> *Id.*

<sup>163</sup> *Id.*

<sup>164</sup> *Id.*

<sup>165</sup> *Id.*

<sup>166</sup> *Id.*

<sup>167</sup> *Id.*

concluded that the plaintiffs sufficiently pleaded the existence of ongoing relationships between the defendants and various medical marketing firms.<sup>168</sup>

The enterprises referred to in the First Coordinated Amended Complaint were not limited to the defendants and various medical marketing firms as they were in the Amended Class Complaint; they had also included physicians who were allegedly paid by these marketing firms to promote off-label uses of Neurontin.<sup>169</sup> Accordingly, the court considered whether physicians who had been paid to promote off-label uses of Neurontin were also part of these enterprises. Neither complaint alleged that these physicians knew that they were part of a “stable” maintained by the drug companies and the medical marketing firms or that they had been acting with other physicians in a coordinated effort to promote Neurontin.<sup>170</sup> However, the complaints did maintain that some of these physicians had had ongoing financial relationships with the defendants and their medical marketing firms and that the physicians had been essential to the success of the defendants’ scheme.<sup>171</sup> Nevertheless, the court concluded that the plaintiffs failed to allege continuing relationships between any specific physicians and specific medical marketing firms sufficient for these physicians to be considered members of a RICO enterprise.<sup>172</sup>

As a result of the court’s refusal to dismiss all of the plaintiffs’ complaints, the case proceeded to discovery, which will likely be hard fought and protracted.<sup>173</sup>

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<sup>168</sup> *Id.*

<sup>169</sup> *Id.*

<sup>170</sup> *Id.*

<sup>171</sup> *Id.*

<sup>172</sup> *Id.* at 184. The plaintiffs alleged that the defendants had engaged in a pattern of racketeering activity by fraudulently promoting off-label uses of Neurontin through the use of interstate mails and wire communications. *Id.* at 177. Thus, the predicate acts alleged were mail fraud and wire fraud. *Id.* at 179. However, the parties did not choose to address the predicate acts requirement at this stage of the proceedings. Instead, the court agreed to allow the plaintiffs to plead the particulars of the defendants’ use of interstate mails and wires after discovery. *Id.* at 184 n.5.

<sup>173</sup> See *In re Neurontin Mktg., Sales Practices & Prod. Liab. Litig.*, 245 F.R.D. 55 (D. Mass. 2007) (overruling an objection to a motion to compel discovery).

## B. *The False Claims Act*

The False Claims Act ("FCA")<sup>174</sup> provides another potential source of liability for drug companies that market their products for off-label uses.

### 1. Elements of the False Claims Act

The False Claims Act is intended to deter the "submission of false or fraudulent claims to the government, to provide restitution to the government for money fraudulently taken from it, and to punish those who defraud the government."<sup>175</sup> The Act imposes liability on any person who "knowingly presents, or causes to be presented, to . . . the United States Government . . . a false or fraudulent claim for payment or approval" or who "knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the Government."<sup>176</sup> The Act further provides that any person who submits a false claim will be liable for treble damages for any loss suffered by the government.<sup>177</sup> In addition, a defendant may be liable for a civil penalty of \$5,000 to \$10,000 for each false claim that he or she submits to the government.<sup>178</sup>

The Act defines "knowingly" to refer to a person who "(1) has actual knowledge of the information; (2) acts in deliberate ignorance of the truth or falsity of the information; or (3) acts in reckless disregard of the truth or falsity of the information . . . ." <sup>179</sup> Thus, innocent mistake and even ordinary negligence are defenses to FCA liability.<sup>180</sup> The FCA does not provide a definition of "claim," but courts have defined it as "a demand for money or for some transfer of public property."<sup>181</sup>

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<sup>174</sup> 31 U.S.C. §§ 3729-3733 (2000).

<sup>175</sup> Lisa Michelle Phelps, Note, *Calling Off the Bounty Hunters: Discrediting the Use of Alleged Anti-Kickback Violations to Support Civil False Claims Actions*, 51 VAND. L. REV. 1003, 1007 (1998). The FCA was enacted during the Civil War to combat procurement fraud and price gouging by army contractors. John Terrence et al., *Clear and Convincing to Whom? The False Claims Act and Its Burden of Proof Standard: Why the Government Needs a Big Stick*, 75 NOTRE DAME L. REV. 1409, 1423 (2000).

<sup>176</sup> 31 U.S.C. §§ 3729(a)(1)-(2).

<sup>177</sup> *Id.* § 3729(a)(7).

<sup>178</sup> *Id.*

<sup>179</sup> 31 U.S.C. § 3729(b).

<sup>180</sup> Pamela H. Bucy, *Growing Pains: Using the False Claims Act to Combat Health Care Fraud*, 51 ALA. L. REV. 57, 61-62 (1999).

<sup>181</sup> *United States v. McNinch*, 356 U.S. 595, 599 (1958).

The term also includes material representations made to avoid paying money owed to the government.<sup>182</sup> Fraud or fraudulent conduct must be material in the sense that it could influence the government's payment decision.<sup>183</sup> In addition, there must be "a causal relationship between the false claim and the government's injury."<sup>184</sup>

The FCA authorizes private individuals, known as relators,<sup>185</sup> to bring *qui tam*<sup>186</sup> actions on behalf of the U.S. government.<sup>187</sup> Relators may be private citizens, employees of government contractors, or employees of government agencies and private companies, including suppliers and competitors of the defendant.<sup>188</sup> In order to maintain a *qui tam* action, the relator must comply with the strict procedural requirements of the FCA.<sup>189</sup> The private plaintiff must, for example, serve a copy of the complaint and disclose substantially all material evidence in the plaintiff's possession to the federal government.<sup>190</sup> Upon receipt of the complaint, the government may investigate the claims and may elect to intervene and take over prosecution of the action.<sup>191</sup> The plaintiff's complaint remains under seal during the government's period of investigation.<sup>192</sup> If the government chooses to intervene, the government itself conducts the civil action.<sup>193</sup> If the government chooses not to intervene in the matter, the private plaintiff has the right to continue to prosecute the case on behalf of the government.<sup>194</sup> However, the relator will not be able to recover attorneys' fees

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<sup>182</sup> 31 U.S.C. § 3729(a)(7).

<sup>183</sup> Joan H. Krause, *Health Care Providers and the Public Fisc: Paradigms of Government Harm Under the Civil False Claims Act*, 36 GA. L. REV. 121, 189 (2001).

<sup>184</sup> *Id.* at 191.

<sup>185</sup> Robert L. Vogel, *The Public Disclosure Bar Against Qui Tam Suits*, 24 PUB. CONT. L.J. 477, 478 (1995).

<sup>186</sup> "*Qui tam*" is short for "qui tam pro domino rege quam pro si ipso in hac parte sequitur," which means "he who sues on behalf of the King as well as for himself." Bucy, *supra* note 180, at 57-58.

<sup>187</sup> 31 U.S.C. § 3730(b).

<sup>188</sup> William E. Kovacic, *Whistleblower Bounty Lawsuits as Monitoring Devices in Government Contracting*, 29 LOY. L.A. L. REV. 1799, 1812 (1996).

<sup>189</sup> See 31 U.S.C. § 3730(b).

<sup>190</sup> *Id.* § 3730(b)(2).

<sup>191</sup> *Id.*

<sup>192</sup> *Id.* This period is at least sixty days, but the DOJ may seek extensions of the sixty-day waiting period. Kovacic, *supra* note 188, at 1817.

<sup>193</sup> 31 U.S.C. § 3730(b)(4)(A).

<sup>194</sup> *Id.* § 3730(b)(4)(B).

or other litigation expenses if he or she is not successful.<sup>195</sup> If the government successfully prosecutes the action, the relator is entitled to between 15% and 25% of the government's recovery,<sup>196</sup> but if the government does not pursue the case and the relator successfully prosecutes it instead, he or she will be awarded between 25% and 30% of the judgment.<sup>197</sup>

Since the FCA's initial passage in 1863, Congress has amended it on several occasions. In 1943, Congress prohibited all *qui tam* actions based on evidence or information that the government had when the action was brought.<sup>198</sup> After the amendment was enacted, there was a significant decrease in the use of the FCA's *qui tam* provisions.<sup>199</sup> Consequently, in 1986, Congress set out to encourage more private enforcement actions by increasing financial awards to private plaintiffs, lowering the plaintiff's burden of proof, and allowing a private plaintiff to participate in actions in which the government elects to intervene.<sup>200</sup> At the same time, in order to discourage "parasitic" lawsuits, Congress added a new jurisdictional provision to the FCA.<sup>201</sup> A *qui tam* suit may be dismissed for lack of jurisdiction if the allegations in the FCA complaint have been previously disclosed publicly or if the lawsuit is based on the publicly disclosed information.<sup>202</sup> Public disclosure may come from such sources as criminal, civil, or administrative hearings; congressional, administrative, or Government Accounting Office reports; hearings, audits, or investigations; and reports in the news media.<sup>203</sup> The issue of whether a *qui tam* action is "based upon" a public disclosure arises "when the information contained in the *qui tam* action has been publicly disclosed, but the relator has not relied upon it in bringing the

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<sup>195</sup> Christopher C. Frieden, Comment, *Protecting the Government's Interests: Qui Tam Actions Under the False Claims Act and the Government's Right to Veto Settlements of Those Actions*, 47 EMORY L.J. 1041, 1051-52 (1998).

<sup>196</sup> 31 U.S.C. § 3730(d)(1).

<sup>197</sup> *Id.* § 3730(d)(2).

<sup>198</sup> Robert Fabrikant & Glenn E. Solomon, *Application of the Federal False Claims Act to Regulatory Compliance Issues in the Health Care Industry*, 51 ALA. L. REV. 105, 107 (1999).

<sup>199</sup> Gregory G. Brooker, *The False Claims Act: Congress Giveth and the Courts Taketh Away*, 25 HAMLINE L. REV. 373, 378-79 (2002).

<sup>200</sup> Krause, *supra* note 183, at 133-34; Frederick M. Morgan, Jr. & Julie Webster Popham, *The Last Privateers Encounter Sloppy Seas: Inconsistent Original-Source Jurisprudence Under the Federal False Claims Act*, 24 OHIO N.U. L. REV. 163, 170 (1998).

<sup>201</sup> Morgan & Popham, *supra* note 200, at 168-69.

<sup>202</sup> Bucy, *supra* note 180, at 88.

<sup>203</sup> 31 U.S.C. § 3730(e)(4) (2000).

*qui tam* action.”<sup>204</sup> The prevailing rule is that a *qui tam* action is “based upon” public disclosure if the action is “supported by” or is “substantially identical” to the publicly disclosed information.<sup>205</sup> However, even if the allegations in the lawsuit are based upon publicly disclosed information, the relator is not barred from bringing a *qui tam* action if he or she is the “original source” of the information.<sup>206</sup> The False Claims Act defines an “original source” as “an individual who has direct and independent knowledge of the information on which the allegations are based and has voluntarily provided the information to the Government before filing an action under this section which is based on the information.”<sup>207</sup>

## 2. *United States ex rel. Franklin v. Parke-Davis*

*United States ex rel. Franklin v. Parke-Davis* serves as an example of how a case may be brought under the FCA against a pharmaceutical manufacturer for the promotion of off-label drug use.<sup>208</sup> The case involved two prescription drugs manufactured by Parke-Davis, Neurontin and Accupril. In 1994, the FDA had approved Neurontin for use as an adjunctive treatment for epilepsy.<sup>209</sup> However, according to the relator, by 1996, more than half of Neurontin sales had been for off-label uses such as pain control, mono-therapy for epilepsy, treatment of bipolar conditions and treatment of attention deficit disorder.<sup>210</sup> Furthermore, half of these off-label uses had been allegedly reimbursed by the federal government either indirectly through Medicaid or directly through purchases by the Veterans Administration (“VA”).<sup>211</sup> The relator also claimed that Parke-Davis had promoted Accupril, an ACE inhibitor approved for the treatment of hypertension and heart failure, for off-label uses.<sup>212</sup>

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<sup>204</sup> Bucy, *supra* note 180, at 95.

<sup>205</sup> *United States ex rel. Precision Co. v. Koch Indus., Inc.*, 971 F.2d 548, 552-53 (10th Cir. 1992).

<sup>206</sup> Bucy, *supra* note 180, at 88-89.

<sup>207</sup> 31 U.S.C. § 3730(e)(4)(B).

<sup>208</sup> *See United States ex rel. Franklin v. Parke-Davis, Div. of Warner-Lambert Co.*, 147 F. Supp. 2d 39 (D. Mass. 2001).

<sup>209</sup> *Id.* at 45.

<sup>210</sup> *Id.*

<sup>211</sup> *Id.*

<sup>212</sup> *Id.*

In 1996, a former employee filed a nine-count *qui tam* action charging that the defendant had engaged in a fraudulent scheme to promote the sale of Neurontin and Accupril for off-label uses and that this illegal marketing campaign had caused numerous false claims to be submitted to the Veterans Administration and to the federal government for reimbursement under its Medicaid program.<sup>213</sup> The complaint remained under seal for several years while the Justice Department decided whether to intervene.<sup>214</sup> Finally, in December of 1999, the complaint was unsealed and the litigation began in earnest.<sup>215</sup> The Justice Department decided to participate only on an *amicus curiae* basis, but reserved the right to intervene as plaintiff at a later date.<sup>216</sup>

The relator, Dr. David Franklin, had been employed by the defendant as a "medical liaison" for about five months during 1996.<sup>217</sup> Although medical liaisons ordinarily work in the research divisions of drug manufacturers, Dr. Franklin claimed that Parke-Davis's medical liaisons were employed exclusively as promotion personnel.<sup>218</sup> According to Franklin, the defendant instructed its medical liaisons "to make exaggerated or false claims concerning the safety and efficacy of Parke-Davis's drugs for off-label uses."<sup>219</sup> Medical liaisons had been encouraged to inflate their scientific credentials and to pose as research personnel instead of sales representatives to bolster their credibility with physicians.<sup>220</sup> Furthermore, when physicians had asked about whether patients could be reimbursed for off-label prescriptions by Medicaid or other insurers, "medical liaisons were instructed to coach doctors on how to conceal the off-label nature of the prescription."<sup>221</sup> The relator also alleged that doctors had received kickbacks for prescribing large quantities of the defendant's products, including cash payments and gifts.<sup>222</sup> Finally, he claimed that Parke-Davis had attempted to conceal its promotion of off-label uses from the FDA by shredding and falsifying documents and by

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<sup>213</sup> *Id.* at 43.

<sup>214</sup> *Id.* at 46.

<sup>215</sup> *Id.*

<sup>216</sup> *Id.* at 46.

<sup>217</sup> *Id.* at 44.

<sup>218</sup> *Id.* at 45.

<sup>219</sup> *Id.*

<sup>220</sup> *Id.*

<sup>221</sup> *Id.* at 46.

<sup>222</sup> *Id.*

encouraging medical liaisons to conduct their marketing activities without leaving a “paper trail” that might be discovered by the FDA.

The first issue the court addressed was the requirement imposed by Federal Rule of Civil Procedure 9(b) that “the circumstances constituting fraud . . . shall be stated with particularity.”<sup>223</sup> This particularity requirement should be read *in pari materia* with Rule 8(a), which allows a plaintiff to make “a short and plain statement” for relief.<sup>224</sup> The court explained that these two provisions, taken together, required the relator to allege the circumstances of the fraud—the “‘who, what, when, where, and how’ of the alleged fraud”—but did not require that he plead all of the evidence or facts that supported his allegation.<sup>225</sup>

Applying these principles to the relator’s Medicaid fraud claims, the court concluded that the complaint, standing alone, lacked the specificity required by Rule 9(b).<sup>226</sup> However, the court allowed the relator to supplement the allegations in his complaint with the more specific information contained in his disclosure to the government pursuant to the FCA in 31 U.S.C. § 3730(b)(2).<sup>227</sup> The disclosure, which had been provided to both the court and the defendant, described Dr. Franklin’s experiences as a “medical liaison” for Parke-Davis and was supported by approximately twenty exhibits.<sup>228</sup> Viewed in light of the relator’s disclosure, the court found that his complaint contained allegations of fraud with respect to the off-label promotion of Neurontin sufficient to satisfy the particularity requirements of Rule 9(b), at least with regard to the Medicaid sales.<sup>229</sup> According to the court, the complaint described a fraudulent scheme designed to increase the submission of off-

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<sup>223</sup> FED. R. CIV. P. 9(b). According to the court, the purpose of Rule 9(b)’s particularity requirement is to enable defendants to prepare a meaningful defense, to prevent conclusory allegations of fraud from serving as a basis for “strike suits and fishing expeditions,” and to protect defendants against groundless charges that may damage their reputations. *Franklin*, 147 F. Supp. 2d at 46 (citing *New England Data Servs., Inc. v. Becher*, 829 F.2d 286, 292 (1st Cir. 1987)).

<sup>224</sup> FED. R. CIV. P. 8(a).

<sup>225</sup> *Franklin*, 147 F. Supp. 2d at 46-47.

<sup>226</sup> *Id.* at 47.

<sup>227</sup> *Id.* The U.S.C. provides that “[a] copy of the complaint and written disclosure of substantially all material evidence and information the person possesses shall be served on the Government pursuant to Rule 4(d)(4) of the Federal Rules of Civil Procedure.” 31 U.S.C. § 3730(b)(2) (2000).

<sup>228</sup> *Franklin*, 147 F. Supp. 2d at 47.

<sup>229</sup> *Id.* at 48.

label Neurontin prescriptions for payment by Medicaid (but not the VA) and identified various false statements made to physicians to induce them to prescribe Neurontin for off-label uses.<sup>230</sup>

As far as the "who" requirement was concerned, the relator's disclosure identified by name various individuals at Parke-Davis who allegedly had instructed the medical liaisons on how to fraudulently promote off-label uses of the drug.<sup>231</sup> In addition, it listed all of the medical liaisons by name, as well as the physicians who had been contacted and given false information and kickbacks in order to encourage them to increase their off-label prescriptions.<sup>232</sup> This was sufficient to satisfy the court. The court determined that the relator also fulfilled the "what" requirement by alleging that the defendant had caused numerous Neurontin prescriptions to be submitted for payment by Medicaid knowing that they were ineligible for payment because they had been prescribed for an off-label use.<sup>233</sup> The "when" requirement was met as well since the relator specified the five-month period during which he had been employed by Parke-Davis.<sup>234</sup> Finally, the court found that the relator fulfilled the "how" requirement by describing in the complaint and the disclosure the defendant's fraudulent marketing campaign involving kickbacks and misleading statements designed to encourage doctors to prescribe Neurontin for unapproved uses.<sup>235</sup>

But the court dismissed the portion of the complaint alleging that Parke-Davis had promoted off-label uses of Neurontin in direct sales to the VA.<sup>236</sup> The court ruled that the relator's allegations were not specific enough because they did not identify which Parke-Davis employees had engaged in fraudulent conduct, where the conduct had taken place, or which VA personnel had been involved.<sup>237</sup> In addition, the complaint failed to identify any specific fraudulent statements that the defendant's employees had made to VA personnel.<sup>238</sup>

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<sup>230</sup> *Id.*

<sup>231</sup> *Id.*

<sup>232</sup> *Id.*

<sup>233</sup> *Id.*

<sup>234</sup> *Id.*

<sup>235</sup> *Id.* The court did not explicitly discuss the "where" requirement, but presumably felt that it was satisfied as well.

<sup>236</sup> *Id.* at 49-50.

<sup>237</sup> *Id.* at 50.

<sup>238</sup> *Id.*

The court also dismissed a count of the complaint alleging that the defendant had illegally promoted off-label uses of Accupril.<sup>239</sup> Specifically, the complaint alleged that Parke-Davis employees had falsely informed physicians that scientific studies had shown Accupril to be more effective than other ACE inhibitors.<sup>240</sup> However, as the court observed, the relator's disclosure did not identify any of the medical liaisons who had been involved in the fraud, any of the doctors who had received false information, or any of the false claims that had been made.<sup>241</sup>

Having concluded that some of the claims against Parke-Davis were specific enough to satisfy Rule 9(b)'s particularity requirement, the court then responded to the defendant's argument that its conduct did not constitute a violation of the False Claims Act.<sup>242</sup> First, the defendant contended that the relator's lawsuit was an improper attempt to use the FCA to create a private cause of action for a violation of the FDCA.<sup>243</sup> The court conceded that Congress did not authorize either the FDA or private individuals to enforce the agency's prohibition against the marketing of drugs for off-label uses through civil actions for damages.<sup>244</sup> However, the court held that the FCA could be invoked to bring a civil action when the violation of an FDA rule or regulation enabled the defendant to obtain a government benefit by fraud.<sup>245</sup> Therefore, a drug manufacturer who knowingly causes a false statement to be made in order to have a false claim paid or approved by the government is subject to liability under the FCA regardless of whether its conduct also violates an FDA regulation.<sup>246</sup>

Parke-Davis also argued that its promotion of off-label uses had not involved the sort of false statement or fraudulent conduct necessary to constitute a violation of the FCA since it had only made *truthful* statements to physicians who provided services to patients covered by Medicaid.<sup>247</sup> However, the court did not need to decide this issue since Parke-Davis was also

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<sup>239</sup> *Franklin*, 147 F. Supp. 2d at 50.

<sup>240</sup> *Id.*

<sup>241</sup> *Id.*

<sup>242</sup> *Id.* at 51-53.

<sup>243</sup> *Id.* at 51.

<sup>244</sup> *Id.*

<sup>245</sup> *Id.* at 51-52.

<sup>246</sup> *Id.* at 52.

<sup>247</sup> *Id.*

accused of engaging in a course of fraudulent conduct, including knowingly making false statements encouraging doctors to submit claims not eligible for payment under the Medicaid program.<sup>248</sup> The FCA claim arose not from the fact that the defendant had promoted off-label uses of its products, but rather from the fact that it had engaged in fraudulent conduct causing claims to be submitted to Medicaid for unauthorized uses.<sup>249</sup>

Furthermore, Parke-Davis maintained that the independent actions of the physicians who wrote the off-label prescriptions and the pharmacists who filled them had been an intervening force that broke the chain of legal causation from the pharmaceutical manufacturer.<sup>250</sup> However, the court pointed out that such an intervening force would break the causal connection only if it were unforeseeable.<sup>251</sup> In this case, the participation of doctors and pharmacists in the submission of false claims to Medicaid had not only been foreseeable but was the intended result of the defendant's fraudulent scheme.<sup>252</sup> Thus, this argument by the defendant was also unavailing.

Finally, Parke-Davis contended that any false statements that it had made to physicians were not material to the government's decision to pay claims for off-label prescriptions of Neurontin.<sup>253</sup> The court, however, noted that a defendant need not make a false claim directly to the government to be held liable under the FCA; it was sufficient in this case for the relator to allege that Parke-Davis had knowingly caused the submission of false claims through a fraudulent course of conduct.<sup>254</sup> The fact that the prescriptions had been for an off-label use was material because the government would not have paid for such prescriptions if it had known the use for which they had been submitted.<sup>255</sup> While the court acknowledged that the relator's theory of liability was somewhat novel and expansive, it concluded that the language of the FCA supports the notion that one who *causes* a false or fraudulent claim to be made may be held liable.<sup>256</sup> The court supported this

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<sup>248</sup> *Id.*

<sup>249</sup> *Id.*

<sup>250</sup> *Id.*

<sup>251</sup> *Id.*

<sup>252</sup> *Id.* at 52-53.

<sup>253</sup> *Id.* at 53.

<sup>254</sup> *Id.*

<sup>255</sup> *Id.*

<sup>256</sup> *Id.*

interpretation of the Act by noting that “the terms of the FCA must be read liberally in accordance with their remedial purpose.”<sup>257</sup>

Thus, the court dismissed some of the counts in the relator’s complaint, but allowed the critical claim to go forward.<sup>258</sup> In 2004, the case was settled when Warner-Lambert, the parent company of Parke-Davis, pleaded guilty to two criminal FDCA misbranding violations and settled the civil cases, ultimately paying \$430 million in criminal fines and civil damages.<sup>259</sup> The relator, Dr. Franklin, received \$24.6 million as part of the settlement between the defendant and the Department of Justice.<sup>260</sup>

### 3. *United States ex rel. Hess v. Sanofi-Synthelabo, Inc.*

The relator in *United States ex rel. Hess v. Sanofi-Synthelabo, Inc.* was less successful than Dr. Franklin in bringing an FCA claim against a pharmaceutical company for promoting off-label uses. In *Hess*, the relator brought a *qui tam* action against his former employer, Sanofi-Synthelabo, alleging that it had fraudulently marketed drugs to physicians for off-label uses.<sup>261</sup> For the reasons explained below, a federal district court dismissed the complaint for failure to state a cause of action pursuant to Rule 12(b)(6) and Rule 9(b).<sup>262</sup>

The relator, who had worked for the defendant as a sales representative from 2001 until 2004, claimed that the defendant had relied upon incomplete, unreliable, and misleading clinical data to promote off-label uses of its drugs Eloxatin and Elitek.<sup>263</sup> In 2002, Eloxatin had been approved by the FDA to help treat fourth-stage colorectal cancer.<sup>264</sup> That same year, the FDA had approved Elitek “for the treatment and prevention of tumor lyses syndrome . . . in pediatric

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<sup>257</sup> *Franklin*, 147 F. Supp. 2d at 53.

<sup>258</sup> *Id.* at 55.

<sup>259</sup> Jack Cinquegrana & Diana K. Lloyd, *Shifting Perspective on Off-Label Promotion*, PHARM. EXECUTIVE, Jan. 1, 2006, [http://www.pharmexec.com/pharmexec/article/articleDetail.jsp?id=282490](http://www.pharmexec.findpharma.com/pharmexec/article/articleDetail.jsp?id=282490).

<sup>260</sup> Evelyn Pringle, *Off-Label Prescribing of Prescription Drugs: Tactics Pfizer Used in Promoting Off-Label Use of Neurontin* (pt. 2), ONLINE J., May 31, 2006, [http://www.onlinejournal.com/artman/publish/article\\_855.shtml](http://www.onlinejournal.com/artman/publish/article_855.shtml).

<sup>261</sup> *United States ex rel. Hess v. Sanofi-Synthelabo, Inc.*, No. 4:05CV570, 2006 WL 1064127, at \*1-2 (E.D. Mo. Apr. 21, 2006).

<sup>262</sup> *Id.* at \*12.

<sup>263</sup> *Id.* at \*1-2.

<sup>264</sup> *Id.* at \*2.

patients," but declined to approve the drug for treatment of the disease in adults.<sup>265</sup> According to the relator, the defendant had provided him and other sales representatives with training on off-label uses of Eloxatin and had instructed them on how Medicare reimbursement for off-label uses of the drug could be obtained.<sup>266</sup> In addition, the relator alleged that the defendant had induced Wisconsin Physician Services ("WPS"), the Medicare administrator for Illinois, Wisconsin, Minnesota, and Michigan, to authorize the use of Eloxatin for the treatment of colorectal cancer in the first line and adjuvant setting even though these were off-label uses at the time.<sup>267</sup> Finally, the relator also claimed that the defendant had briefed him and other sales representatives about off-label uses of Elitek in adult patients and had encouraged them to promote off-label uses of the drug.<sup>268</sup>

In its motion to dismiss, the defendant contended that the relator failed to allege that it had made any misrepresentations to doctors, the government, or anyone else regarding Eloxatin. Nor did the relator allege that any doctor had prescribed Eloxatin improperly or that any doctor who had prescribed Eloxatin had made any misrepresentations to Medicare in order to obtain reimbursement for off-label uses of the drug. Furthermore, the relator did not allege that the information provided by the defendant about off-label uses of Elitek had been either false or deceitful.<sup>269</sup>

In the case of Eloxatin, the court acknowledged that physicians had filed claims for Medicare reimbursement for off-label uses of the drug.<sup>270</sup> The court also agreed that the FCA is broad enough to impose liability on a drug company who knowingly assists the government to pay fraudulent claims to a third person even if the drug company does not have any direct contractual relations with the government.<sup>271</sup> However, the court cautioned that in order to state a valid claim under the FCA, the relator must show that the defendant made a

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<sup>265</sup> *Id.*

<sup>266</sup> *Id.*

<sup>267</sup> *Id.*

<sup>268</sup> *Id.* The FDA subsequently approved Eloxatin for treatment of colorectal cancer in the first line and adjuvant settings after the defendant submitted supplemental New Drug Applications for these uses. *Id.*

<sup>269</sup> *Id.* at \*4.

<sup>270</sup> *Id.* at \*7.

<sup>271</sup> *Id.* (citing *United States ex rel. Franklin v. Parke-Davis*, 147 F. Supp. 2d 39, 48 (D. Mass. 2001)).

*material* misrepresentation.<sup>272</sup> To satisfy this materiality requirement, the relator had to allege, with the required specificity, (1) that the defendant had fraudulently promoted certain off-label uses of Eloxatin to doctors; (2) that these doctors had submitted Medicare claims for these off-label uses; and (3) that these claims had resulted from the defendant's promotion of the off-label uses.<sup>273</sup> Thus, the relator had to show that but for the defendant's fraudulent misrepresentations, the doctors would not have made claims to Medicare for off-label uses of Eloxatin and that but for these fraudulent misrepresentations, Medicare would not have reimbursed the doctors.<sup>274</sup>

The court concluded that the relator failed to establish this causal connection. The relator alleged that although Eloxatin had only been approved for second-line treatment of fourth stage colorectal cancer, the defendant had encouraged physicians to submit Medicare claims for other stages of colorectal cancer.<sup>275</sup> The court noted that although the Medicare reimbursement form did have a line for a patient's diagnosis, it did not require doctors to indicate the stage of a patient's cancer.<sup>276</sup> Therefore, the court concluded that the stage of cancer was not material to either the doctor's Medicare reimbursement claim or to the government's decision to pay the claim.<sup>277</sup> Thus, the defendant's conduct had not caused false claims to be made to the government.

The court then considered whether the relator had pleaded sufficient evidence of intent as required by the FCA. The FCA requires that there be "actual knowledge that the information was untrue or deliberate ignorance or reckless disregard of the truth or falsity of that information" on the part of the defendant.<sup>278</sup> The court determined that the relator did not allege that the defendant had deliberately lied to either its sales staff or to the doctors who prescribed Eloxatin. Nor did the relator claim that the information the defendant had disseminated about off-label uses was incorrect or false.<sup>279</sup> Instead, he merely alleged that the information was

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<sup>272</sup> *Hess*, 2006 WL 1064127, at \*7.

<sup>273</sup> *Id.*

<sup>274</sup> *Id.*

<sup>275</sup> *Id.* at \*2.

<sup>276</sup> *Id.*

<sup>277</sup> *Id.*

<sup>278</sup> *Id.* at \*9 (quoting *United States v. Taber*, 342 F.3d 843, 845 (8th Cir. 2003)).

<sup>279</sup> *Id.*

"immature, unreliable and misleading."<sup>280</sup> Nor did the relator allege that the defendant had assisted doctors to make fraudulent claims. As the court already concluded, the Medicare reimbursement for off-label uses of Eloxatin had not been fraudulent because the alleged off-label use was for the treatment of an earlier stage of colorectal cancer and the Medicare forms in question did not require doctors to identify the stage of a patient's cancer.<sup>281</sup> Consequently, the court concluded that the relator's complaint failed to satisfy the FCA's intent requirement.<sup>282</sup>

With regard to Elitek, the court found that the only factual allegations the relator made to support his claim were that the defendant had informed him and other sales representatives about off-label uses of the drug, had encouraged them to promote these off-label uses, and had pressured them to derive a substantial amount of Elitek sales from these off-label uses.<sup>283</sup> However, the court also determined that the relator's complaint failed to identify the time or place of the allegedly false representations regarding Elitek, nor did it describe the nature or content of the claims that it alleged had been fraudulent.<sup>284</sup> Furthermore, the relator failed to allege that the doctors to whom the defendant's sales representatives promoted off-label uses of Elitek actually had submitted false claims to the government for such uses.<sup>285</sup> Instead, the relator's allegations were "vague, conclusory, and lack[ed] the requisite specificity to withstand a motion to dismiss pursuant to either Rule 12(b)(6) or Rule 9(b)."<sup>286</sup> Accordingly, the court granted the defendant's motion to dismiss the relator's claims regarding Elitek.

Finally, the court rejected the relator's argument that the defendant should be found liable under 31 U.S.C. § 3729(a)(3) of the FCA, which creates liability for persons who conspire to defraud the government through fraudulent claims or payments.<sup>287</sup> According to the court, to state a claim for conspiracy:

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<sup>280</sup> *Id.*

<sup>281</sup> *Id.*

<sup>282</sup> *Id.*

<sup>283</sup> *Id.* at \*6.

<sup>284</sup> *Id.*

<sup>285</sup> *Id.*

<sup>286</sup> *Id.*

<sup>287</sup> *Id.* at \*11.

[A] plaintiff must allege: “(1) that the defendant conspired with one or more persons to get a false or fraudulent claim allowed or paid by the United States, and (2) that one or more conspirators performed any act to effect the object of the conspiracy, and (3) that the United States suffered damages as a result of the false or fraudulent claim.”<sup>288</sup>

In this case, the relator did not plead facts suggesting that physicians had provided fraudulent or false information to the government or that the defendant had provided such information to the physicians.<sup>289</sup> Moreover, the court found that the relator did not allege any facts indicating that the defendant had acted in concert with physicians to make false or fraudulent claims to the government.<sup>290</sup> Finding that the relator’s allegation of a conspiracy did not meet the particularity requirements of Rule 9(b), the court ruled that the conspiracy claim should be dismissed as well.<sup>291</sup> Thus, the court dismissed the relator’s complaint in its entirety.<sup>292</sup>

*Hess* illustrates the challenges plaintiffs face when they bring *qui tam* actions against drug companies under the FCA. In particular, both the materiality requirement and the intent requirement of the Act present significant obstacles to success.

#### 4. *United States ex rel. Rost v. Pfizer, Inc.*

*United States ex rel. Rost v. Pfizer, Inc.* provides a third example of how an FCA claim may be brought against a pharmaceutical company that has promoted off-label uses. The relator in this case, Dr. Peter Rost, brought a *qui tam* action against Pfizer and Pharmacia Corporation, which had been acquired by Pfizer in 2003, alleging that they had engaged in illegal off-label marketing of the drug Genotropin and had knowingly caused false claims to be submitted to federal and state health insurance programs.<sup>293</sup> The alleged fraudulent conduct had taken place between 1997 and 2003.<sup>294</sup> The defendants moved to dismiss the complaint, arguing that the

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<sup>288</sup> *Hess*, 2006 WL 1064127, at \*11 (quoting *Corsello v. Lincare, Inc.*, 428 F.3d 1008, 1014 (11th Cir. 2005)).

<sup>289</sup> *Id.*

<sup>290</sup> *Id.*

<sup>291</sup> *Id.*

<sup>292</sup> *Id.* at \*12.

<sup>293</sup> *United States ex rel. Rost v. Pfizer, Inc. (Rost I)*, 446 F. Supp. 2d 6, 8-10 (D. Mass. 2006), *vacated and remanded*, *Rost v. Pfizer, Inc. (Rost II)*, 507 F.3d 720 (1st Cir. 2007).

<sup>294</sup> *Id.* at 10.

court lacked subject matter jurisdiction because of the public disclosure bar and that the claim failed to allege fraud with sufficient particularity to satisfy Rule 9(b).<sup>295</sup> The district court rejected the claim that the public disclosure bar applied,<sup>296</sup> but, like the *Hess* court, dismissed the relator's case because his allegations were not sufficiently specific to meet the requirements of Rule 9(b).<sup>297</sup> On appeal, the First Circuit agreed with the conclusions of the trial court, but held that the relator should be given a chance to amend his complaint.<sup>298</sup>

Genotropin is a recombinant or man-made human growth hormone that had been approved by the FDA to treat certain hormonal deficiencies in both adults and children.<sup>299</sup> The FDA had not approved the drug as a treatment for short children without hormonal deficiencies or as an anti-aging treatment for adults.<sup>300</sup> However, the relator alleged that, beginning in 1997, Pharmacia marketed Genotropin to increase growth in short children and to delay the aging process in adults.<sup>301</sup> Pharmacia had given bribes, kickbacks, and other incentives to doctors to prescribe Genotropin and to wholesale drug distributors to recommend Genotropin for off-label uses.<sup>302</sup> The company also had rewarded sales representatives for every new Genotropin patient, regardless of whether the prescription was for an approved or an off-label use.<sup>303</sup> As a result of these marketing efforts, approximately sixty percent of adult sales and twenty-five percent of pediatric sales of Genotropin had been for off-label uses during this period.<sup>304</sup>

As manager of Pharmacia's Endocrine Care Unit, Dr. Rost had overseen the worldwide marketing of Genotropin, but had not been involved in the day-to-day marketing or sales of the drug.<sup>305</sup> However, when he learned of Pharmacia's off-label marketing of Genotropin, Dr. Rost had unsuccessfully tried to put a stop to the practices.<sup>306</sup> When Pfizer acquired Pharmacia,

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<sup>295</sup> *Id.* at 11, 15, 25.

<sup>296</sup> *Id.* at 25.

<sup>297</sup> *Id.* at 28.

<sup>298</sup> *Rost II*, 507 F.2d 720, 723.

<sup>299</sup> *Rost I*, 446 F. Supp. 2d. at 10.

<sup>300</sup> *Id.*

<sup>301</sup> *Id.*

<sup>302</sup> *Id.*

<sup>303</sup> *Id.*

<sup>304</sup> *Id.*

<sup>305</sup> *Id.* at 9.

<sup>306</sup> *Id.* at 10.

it confirmed the relator's charges and notified senior officials at the FDA and the Office of the Inspector General about the off-label marketing.<sup>307</sup> In 2003, while the FDA was still investigating the Genotropin issue, the relator filed a *qui tam* action alleging fraud in the off-label marketing of Genotropin by Pharmacia.<sup>308</sup> In late 2005, the DOJ decided not to intervene in the case, leaving Dr. Rost to proceed on his own.<sup>309</sup>

The defendant moved to dismiss the claim for lack of subject matter jurisdiction based on the FCA's "public disclosure bar."<sup>310</sup> In its decision, the trial court declared that it must determine whether the allegations of fraud in the complaint were "publicly disclosed" before the relator filed his lawsuit and whether the allegations were "based upon" that disclosure.<sup>311</sup> The relator argued that the defendants' voluntary disclosures had not amounted to a "public disclosure" because they had not been disclosed in a statutorily required manner.<sup>312</sup> The court agreed, finding that the public disclosure bar prohibited *qui tam* actions only when the plaintiff's allegations were "based upon the public disclosure of allegations or transactions in a criminal, civil, or administrative hearing, in a congressional, administrative, or Government Accounting Office report, hearing, audit, or investigation, or from the news media . . . ."<sup>313</sup>

The court observed that Congress intended the public disclosure bar to prohibit only truly parasitic lawsuits.<sup>314</sup> Actions in which the disclosed information lies only in the hands of the government and the party who disclosed it to the government are not parasitic.<sup>315</sup> In other words, a *qui tam* action is not parasitic when a private plaintiff does not, and cannot, know what information may already be in the government's possession.<sup>316</sup> Consequently, the court ruled that the defendants' voluntary disclosure of information to various

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<sup>307</sup> *Rost I*, 446 F. Supp. 2d. at 10.

<sup>308</sup> *Id.* at 11.

<sup>309</sup> *Id.*

<sup>310</sup> 31 U.S.C. § 3730(e)(4)(A) (2000). The FCA's "public disclosure bar" provides for the dismissal of *qui tam* actions that are based on information that has already been disclosed to the public. *See supra* text accompanying notes 203-207.

<sup>311</sup> *Rost I*, 446 F. Supp. 2d at 15.

<sup>312</sup> *Id.*

<sup>313</sup> *Id.* at 18 (quoting 31 U.S.C. § 3730(e)(4)(A) (1994)).

<sup>314</sup> *Id.*

<sup>315</sup> *Id.*

<sup>316</sup> *Id.*

government officials did not constitute a public disclosure for purposes of the FCA's jurisdictional bar.<sup>317</sup>

On appeal, the First Circuit agreed that disclosures made by Pfizer to the government would not prevent the relator from bringing his suit against the pharmaceutical company under the public disclosure bar of the FCA.<sup>318</sup> According to the court:

In our view, a "public disclosure" requires that there be some act of disclosure to the public outside of the government. The mere fact that the disclosures are contained in government files someplace, or even that the government is conducting an investigation behind the scenes, does not itself constitute public disclosure. Our construction of the term "public disclosure" does not turn on the fact that Pfizer requested or assumed that its disclosures to the investigating agencies would be held confidential.<sup>319</sup>

The appeals court also declared that Pfizer's position was "inconsistent with our understanding of the language, structure, and history of the [False Claims] Act."<sup>320</sup> According to the court, the FCA's public disclosure provision was intended to prevent relators from bringing *qui tam* actions "based on information made available to the public during the course of a government hearing, investigation, or audit."<sup>321</sup> Elaborating on the distinction between disclosure to the government and disclosure to the public, the court observed that § 3730 uses the term "government" many times but never in a sense synonymous with the public.<sup>322</sup> Reviewing the FCA's legislative history, the court pointed out that the 1986 amendments removed a provision that barred private lawsuits whenever the government was aware of the allegations or transactions set forth in the relator's complaint.<sup>323</sup> The court reasoned that those amendments reflected Congress's determination that the earlier version of § 3730 unduly restricted private enforcement of the FCA.<sup>324</sup>

The court rejected the argument that Pfizer's proposed government knowledge bar was nevertheless consistent with

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<sup>317</sup> *Id.*

<sup>318</sup> *Rost II*, 507 F.3d 720, 728 (1st Cir. 2007).

<sup>319</sup> *Id.*

<sup>320</sup> *Id.*

<sup>321</sup> *Id.* at 729 (quoting *United States ex rel. LeBlanc v. Raytheon Co.*, 913 F.2d 17, 20 (1st Cir. 1990)).

<sup>322</sup> *Id.*

<sup>323</sup> *Id.*

<sup>324</sup> *Id.*

congressional intent because it would only apply in limited circumstances.<sup>325</sup> Relying on a Seventh Circuit case, Pfizer contended that a government knowledge bar based on § 3730 only applies where the government official to whom the disclosure is made is the appropriate investigatory official.<sup>326</sup> However, the court declared that it could “find no support in either the language or the history of the statute for such a reading.”<sup>327</sup> Furthermore, the court concluded that Pfizer’s argument was inconsistent with its opinion in *United States ex rel. S. Praver & Co. v. Fleet Bank of Maine*, which held that “Congress has explicitly deemed a ‘notice’ regime insufficient to protect the government against false claims (indeed it was *precisely such a regime* that Congress sought to abandon in enacting the 1986 amendments) . . . .”<sup>328</sup>

Furthermore, the court declared that Pfizer’s proposed government knowledge bar would conflict with another objective embodied in the 1986 amendments: “to help keep the government honest in its investigations and settlements with industry.”<sup>329</sup> According to the court, once a relator’s allegations are made public, the government can be forced by public pressure to pursue false claims investigations that it might otherwise prefer to ignore.<sup>330</sup> However, fewer *qui tam* actions would be brought, and thus less information would be made available to the public, if private *qui tam* actions were barred by a government knowledge rule such as that proposed by Pfizer.

In addition, the court suggested that Pfizer’s proposed government knowledge rule would not be consistent with Congress’s goal of discouraging “parasitic” *qui tam* actions.<sup>331</sup> By prohibiting *qui tam* actions based on information that is kept confidential by government officials, Pfizer’s interpretation would not only fail to discourage parasitic lawsuits, but would also discourage legitimate suits by relators based on “direct and independent knowledge” of wrongdoing.<sup>332</sup> Finally,

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<sup>325</sup> *Rost II*, 507 F.3d at 730.

<sup>326</sup> *Id.* (citing *United States ex rel. Mathews v. Bank of Farmington*, 166 F.3d 853, 861 (7th Cir. 1999)).

<sup>327</sup> *Id.*

<sup>328</sup> *Id.* (emphasis in original) (quoting *United States ex rel. S. Praver & Co. v. Fleet Bank of Me.*, 24 F.3d 320, 329 (1st Cir. 1994)).

<sup>329</sup> *Id.*

<sup>330</sup> *Id.*

<sup>331</sup> *Id.*

<sup>332</sup> *Id.*

the court observed that several other circuits had rejected similar constructions of the government knowledge rule.<sup>333</sup>

The second issue in *Rost* was whether the relator had pleaded his claim of fraud with sufficient particularity to satisfy the requirements of Rule 9(b)—a familiar issue in FCA litigations.<sup>334</sup> The trial court acknowledged that the relator's complaint provided a great amount of detail about the defendants' illegal marketing, promotion, and distribution of Genotropin as well as the bribes, kickbacks, and other financial incentives that the defendants had provided to distributors and physicians.<sup>335</sup> However, the court also found that the complaint failed to identify any actual false claims that had been submitted to the government for reimbursement of off-label prescriptions of Genotropin.<sup>336</sup> Instead, the relator had simply assumed that the defendants' illegal marketing efforts must have caused at least some physicians to prescribe Genotropin for off-label uses and that at least some of these prescriptions must have been reimbursed by federal or state health care programs.<sup>337</sup> Because the relator failed to plead the existence of false claims made to the government with sufficient particularity, the trial court dismissed the complaint pursuant to Rule 9(b).<sup>338</sup>

On appeal, Dr. Rost argued that the trial court had interpreted Rule 9(b)'s particularity requirements too strictly.<sup>339</sup> In response, Pfizer argued that the result below was mandated by the First Circuit's decision in *United States ex rel. Karvelas v. Melrose-Wakefield Hospital*.<sup>340</sup> The *Karvelas* court had ruled that "a *qui tam* relator may not present general allegations in lieu of the details of actual false claims in the hope that such

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<sup>333</sup> *Id.* (citing *Kennard v. Comstock Res., Inc.*, 363 F.3d 1039, 1043 (10th Cir. 2004); *United States ex rel. Schumer v. Hughes Aircraft Co.*, 63 F.3d 1512, 1518 (9th Cir. 1995), *vacated on other grounds*, 520 U.S. 939 (1997) (holding that the 1986 FCA amendment does not apply retrospectively to prior acts); *United States ex rel. Williams v. NEC Corp.*, 931 F.2d 1493, 1496 n.7 (11th Cir. 1991)). Only the Seventh Circuit, in *United States ex rel. Mathews v. Bank of Farmington*, has adopted the government knowledge approach. *Id.* at 731 (citing *Mathews*, 166 F.3d at 861). The *Rost II* court declared, "We simply disagree with *Mathews* for the reasons already stated and as lucidly set forth in the district court's opinion." *Id.*

<sup>334</sup> *Id.* at 731-34.

<sup>335</sup> *Rost I*, 446 F. Supp. 2d at 27.

<sup>336</sup> *Id.*

<sup>337</sup> *Id.* at 27-28.

<sup>338</sup> *Id.*

<sup>339</sup> *Rost II*, 507 F.3d at 731.

<sup>340</sup> *Id.* (citing *United States ex rel. Karvelas v. Melrose-Wakefield Hosp.*, 360 F.3d 220 (1st Cir. 2004)).

details will emerge through subsequent discovery.”<sup>341</sup> The relator in that case alleged that his employer, a hospital, had submitted claims to government health care programs for services that were “provided improperly or not at all.”<sup>342</sup> The court dismissed the relator’s complaint because it provided no specifics about particular false claims for payments that may have been made.<sup>343</sup> Nevertheless, the Circuit Court in *Rost* found that *Karvelas* provided that the requirements of Rule 9(b) may be satisfied even though some questions remained if the complaint as a whole is sufficiently particular to fulfill FCA pleading requirements.<sup>344</sup> However, even giving the relator in *Rost* the benefit of this flexibility, the court still concluded that his claim failed to satisfy the pleading requirements of Rule 9(b).<sup>345</sup>

The court pointed out that, unlike in *Karvelas*, any false claims in *Rost* would have been submitted to the government by individual doctors and hospitals, not by the defendant, Pfizer.<sup>346</sup> Thus, it would be difficult, if not impossible, for the relator, Dr. Rost, to have had personal knowledge that false claims had been submitted by third parties. Given the fact that a substantial percentage of Genotropin prescriptions were written for off-label uses, it was highly probable that at least some of these prescriptions had been paid for by federal health care programs.<sup>347</sup> However, the court observed that the relator’s position was somewhat undermined by a statement in the criminal information against Pfizer to the effect that most patients who take the drug for off-label purposes “paid out-of-pocket without reimbursement from any public or private third-party payors.”<sup>348</sup> After taking this offsetting evidence into account, the court concluded that the allegations contained in the relator’s complaint did not satisfy the particularity requirements of Rule 9(b):

At most, Rost raises facts that suggest fraud was possible; but the complaint contained no factual or statistical evidence to strengthen the inference of fraud beyond possibility. It may well be that doctors

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<sup>341</sup> *Karvelas*, 360 F.3d at 231.

<sup>342</sup> *Id.* at 223.

<sup>343</sup> *Id.* at 233-35.

<sup>344</sup> *Rost II*, 507 F.3d at 732 (citing *Karvelas*, 360 F.3d at 233 n.17).

<sup>345</sup> *Id.*

<sup>346</sup> *Id.*

<sup>347</sup> *Id.*

<sup>348</sup> *Id.*

who prescribed Genotropin for off-label uses as a result of Pharmacia's illegal marketing of the drug withstood the temptation and did not seek federal reimbursement, and neither did their patients. It may be that physicians prescribed Genotropin for off-label uses only where the patients paid for it themselves or when the patients' private insurers paid for it. Rost did not plead enough to satisfy the concerns behind Rule 9(b).<sup>349</sup>

Consequently, the First Circuit affirmed the trial court's Rule 9(b) ruling.<sup>350</sup>

Finally, the court considered whether Dr. Rost should be given an opportunity to amend his complaint in order to satisfy the particularity requirements of Rule 9(b).<sup>351</sup> The court observed that Rule 15(a) provides that leave to amend a pleading "shall be freely given when justice so requires."<sup>352</sup> Refraining from making an initial determination on the futility of amendment, the court remanded for further consideration on this issue.<sup>353</sup>

The *Rost* case serves as another illustration that the FCA can be a source of liability for manufacturers that promote off-label uses. However, relators that wish to bring such claims may have a tough time meeting the particularity requirement of Rule 9(b) for alleging fraud.

##### 5. *United States ex rel. Richardson v. Bristol-Myers Squibb*

One of the most recent False Claims Act cases involved the Bristol-Myers Squibb Company ("BMS"). In September, 2007, BMS and its wholly-owned subsidiary Apothecon, Inc., reached a \$515 million dollar settlement with the Department of Justice.<sup>354</sup> The settlement resolved seven *qui tam* actions brought against BMS and Apothecon under the FCA.<sup>355</sup> According to the government, between the years 2000 and 2003 BMS had paid doctors and other health care providers to

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<sup>349</sup> *Id.* at 733.

<sup>350</sup> *Id.*

<sup>351</sup> *Id.* at 733-34.

<sup>352</sup> *Id.* at 733 (quoting FED. R. CIV. P. 15(a)).

<sup>353</sup> *Id.* at 734.

<sup>354</sup> Press Release, U.S. Department of Justice, Bristol-Myers Squibb to Pay More Than \$515 Million to Resolve Allegations of Illegal Drug Marketing and Pricing 1 (Sept. 28, 2007), available at [http://www.usdoj.gov/opa/pr/2007/September/07\\_civ\\_782.html](http://www.usdoj.gov/opa/pr/2007/September/07_civ_782.html).

<sup>355</sup> *Id.* at 2

purchase BMS pharmaceutical products.<sup>356</sup> This illegal remuneration had included payments to physicians and others to enable them to participate in consulting programs, advisory boards, and preceptorships, often involving travel to luxury resorts.<sup>357</sup> The government also claimed that BMS had knowingly promoted Abilify, an anti-psychotic drug, to treat pediatric patients and to treat dementia-related psychosis in geriatric patients—both of which were unapproved, off-label uses.<sup>358</sup> The company's sales representatives had allegedly urged child psychiatrists and pediatricians to prescribe Abilify to their patients.<sup>359</sup> BMS had also assembled a specialized sales force that directed its attention almost entirely toward nursing homes that were likely to have large numbers of patients with dementia-related psychosis.<sup>360</sup>

Pursuant to a settlement agreement, the federal government recovered over \$320 million, including a \$25 million “disgorgement” of illegal profits arising from BMS's illegal promotion of Abilify for off-label uses.<sup>361</sup> In addition, BMS was required to pay \$187 million to state Medicaid participants and \$124,000 to certain other public health agencies.<sup>362</sup>

Although the outcomes of the cases discussed above are mixed, it is clear that the False Claims Act represents a serious threat to drug companies that illegally promote off-label uses of their products. Both relators and the federal government are aggressively pursuing FCA cases against drug companies, and some of these companies have been forced to pay hundreds of millions of dollars in settlements.

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<sup>356</sup> *Id.* at 1.

<sup>357</sup> *Id.*

<sup>358</sup> *Id.* at 2.

<sup>359</sup> *Id.*

<sup>360</sup> *Id.* In addition, the government alleged that BMS and Apoteco had charged fraudulent and inflated prices for many of its oncology and generic drugs, knowing that the reimbursement rates provided by federal health care programs would be based on these higher prices. *Id.* Finally, the government charged that BMS had knowingly misreported its best price for the anti-depression drug Serzone by failing to include in its calculations lower-priced sales of the drug to a large commercial purchaser. *Id.* This action caused Medicaid and other public health providers, who were entitled to purchase drugs at the manufacturer's “best price,” to pay more for these products than they would have if BMS's best price information had been accurate. *Id.*

<sup>361</sup> *Id.*

<sup>362</sup> *Id.* Finally, BMS agreed to sign a corporate integrity agreement with the Department of Health and Human Services that requires it to report accurate average sales prices and average manufacturer prices for all of its products that are covered by Medicare or other federal health care programs.

#### IV. TORT LIABILITY FOR PROMOTION OF OFF-LABEL USES

Tort liability is the final pitfall for drug and medical device manufacturers that encourage physicians to make off-label uses of their products. Of course, drug manufacturers are subject to liability for product-related injuries when their products are used for their intended purposes if they are defectively manufactured or designed or when the warnings provided are inadequate.<sup>363</sup> However, additional theories of tort liability may be available to plaintiffs when they are injured by off-label uses of prescription drugs or medical devices. This portion of the Article examines four tort-based claims: (1) claims based on violations of the FDCA, including fraud-on-the-FDA and negligence per se claims, (2) claims arising from fraudulent misrepresentation and improper marketing practices, (3) claims based on failure to warn, and (4) claims based on failure to test.

##### A. *Tort Claims Based on Violations of the FDCA*

Plaintiffs are increasingly basing their claims against producers of drugs and medical devices on alleged violations of the Food, Drug and Cosmetic Act or regulations promulgated by the FDA pursuant to the Act.<sup>364</sup> At first, plaintiffs had often alleged that the defendants were guilty of "fraud-on-the-FDA." However, more recently, they have tended to argue that violations of the FDCA constitute "negligence per se."

##### 1. Fraud on the FDA

There is general agreement that the FDCA does not authorize lawsuits by private individuals to enforce its provisions.<sup>365</sup> Nevertheless, during the 1990s, a number of lawsuits

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<sup>363</sup> RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIAB. § 6 (1998).

<sup>364</sup> James M. Beck & John A. Valentine, *Challenging the Viability of FDCA-Based Causes of Action in the Tort Context: The Orthopedic Bone Screw Experience*, 55 FOOD & DRUG L.J. 389, 389 (2000).

<sup>365</sup> See, e.g., *In re Orthopedic Bone Screw Prods. Liab. Litig. (Bone Screw I)*, 159 F.3d 817, 824 (3d Cir. 1998), *rev'd*, *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001); *PDK Labs., Inc. v. Friedlander*, 103 F.3d 1105, 1113 (2d Cir. 1997); *Bailey v. Johnson*, 48 F.3d 965, 967-68 (6th Cir. 1995); *Mylan Labs., Inc. v. Matkari*, 7 F.3d 1130, 1139 (4th Cir. 1993); *Pacific Trading Co. v. Wilson & Co.*, 547 F.2d 367, 370-71 (7th Cir. 1976); *Griffin v. O'Neal, Jones & Feldman, Inc.*, 604 F. Supp. 717, 718 (S.D. Ohio 1985); *Nat'l Women's Health Network, Inc. v. A.H. Robins Co.*, 545 F. Supp. 1177, 1178 (D. Mass. 1980); *Keil v. Eli Lilly & Co.*, 490 F. Supp. 479, 480 (E.D. Mich. 1980).

were brought against the manufacturers of various spinal fixation implant devices<sup>366</sup> alleging that these manufacturers had lied to the FDA in order to obtain permission to market their products.<sup>367</sup> Specifically, these plaintiffs contended that the manufacturers of fixation implant devices had assured the FDA that their devices would be marketed for bone surgeries and other approved uses when in fact the manufacturers had intended to market them for an off-label use as pedicle spinal implant devices.<sup>368</sup> The plaintiffs claimed that by making these false assurances to the FDA, the manufacturers had been able to obtain approval for these devices under the premarket notification process<sup>369</sup> instead of the more lengthy and

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<sup>366</sup> In spinal fusion surgery, bone graft material, usually taken from the patient's hipbone, is inserted between two vertebrae to create a single immobile block to reduce the pain caused when vertebrae move in different directions. *Valente v. Sofamor, S.N.C.*, 48 F. Supp. 2d 862, 864 (E.D. Wis. 1999). The rods are attached to vertebrae by spine-hooks, wires, or metal screws (known as bone screws) that are inserted into the pedicles of neighboring vertebrae and connected to rods or plates to reduce movement between these vertebrae. *Cali v. Danek Med., Inc.*, 24 F. Supp. 2d 941, 945 (W.D. Wis. 1998). If the spinal fusion surgery is successful, the bone graft and the vertebrae fuse together to form a single bony mass. *Minisan v. Danek Med., Inc.*, 79 F. Supp. 2d 970, 972 (N.D. Ind. 1999). Once this occurs, the spinal fixation device can be removed. *Menges v. Depuy Motech, Inc.*, 61 F. Supp. 2d 817, 822 (N.D. Ind. 1999). Pedicles are two rearward facing bony arches on either side of the vertebrae that support the lamina. *Minisan*, 79 F. Supp. 2d at 972 n.1.

Various types of bone screw fixation devices have been the subject of litigation. These include AcroMed's Variable Screw Placement ("VSP") Device (*Bone Screw I*, 159 F.3d at 821; *Reeves v. AcroMed Corp.*, 44 F.3d 300, 303-04 (5th Cir. 1995); *Dutton v. AcroMed Corp.*, 691 N.E.2d 738, 740 (Ohio Ct. App. 1997)); Artifex's HBH Spinal System (*Sharp v. Artifex, Ltd.*, 110 F. Supp. 2d 388, 389 (W.D. Pa. 1999)); Danek's Texas Scottish Rite Hospital ("TSRH") Spinal System Device (*Minisan*, 79 F. Supp. at 972; *Sita v. Danek Med., Inc.*, 43 F. Supp. 2d 245, 249-50 (E.D.N.Y. 1999); *King v. Danek Med., Inc.*, 37 S.W.3d 429, 431 (Tenn. Ct. App. 2000)); Danek's Dyna-Lok Device (*Talley v. Danek Med., Inc.*, 179 F.3d 154, 155-56 (4th Cir. 1999)); Danek's Luque System (*Cali*, 24 F. Supp. 2d at 946); Smith & Nephew Richards's Rogozinski System (*Blinn v. Smith & Nephew Richards, Inc.*, 55 F. Supp. 2d 1353, 1356 (M.D. Fla. 1999)); and Sofamor's Cotrel Dubousset System (*Smith v. Sofamor, S.N.C.*, 21 F. Supp. 2d 918, 919 (W.D. Wis. 1998)).

<sup>367</sup> *Bone Screw I*, 159 F.3d at 820; *Reeves*, 44 F.3d at 303-04; *Dutton*, 691 N.E.2d at 740 (Ohio Ct. App. 1997); see also *Kemp v. Medtronic, Inc.*, 231 F.3d 216, 232-33 (6th Cir. 2000) (cardiac pacemaker).

<sup>368</sup> *Bone Screw I*, 159 F.3d at 820; *Reeves*, 44 F.3d at 306; *Dutton*, 691 N.E.2d at 740.

<sup>369</sup> The Medical Device Amendments provide that medical devices that are "substantially equivalent" to an existing approved device can secure marketing authorization from the FDA through a premarket notification, or § 510(k), process. 21 U.S.C. 360(k)-(o) (2006); U.S. Food and Drug Admin., Premarket Notification 510(K), <http://www.fda.gov/CDRH/DEVADVICE/314.html>. For a discussion of the premarket notification process, see Richard C. Ausness, "After You, My Dear Alphonse!": *Should the Courts Defer to the FDA's New Interpretation of § 360k(a) of the Medical Device Amendments?*, 80 TUL. L. REV. 727, 733 (2006); see also Trent Kirk, Comment, *Fraud-on-the-FDA & Buckman—The Evolving Law of Federal Preemption in Products Liability Litigation*, 53 S.C. L. REV. 673, 681 (2002).

expensive premarket approval procedure ("PMA").<sup>370</sup> Under the fraud-on-the-FDA theory, the devices in question would never have been marketed in the absence of this fraud and therefore the manufacturers should be liable for any resulting injuries, even though the plaintiffs could not prove that the devices were defective.<sup>371</sup>

Until 2001, there was a split of authority over whether fraud-on-the-FDA claims were preempted by the Medical Device Amendments to the FDCA.<sup>372</sup> The U.S. Supreme Court resolved this conflict in *Buckman Co. v. Plaintiffs' Legal Committee*.<sup>373</sup> The plaintiffs in *Buckman* contended that they had been injured by surgical bone screws manufactured by AcroMed Corporation.<sup>374</sup> They alleged that the manufacturer and its consultant, the Buckman Company, had obtained FDA approval to market the screws as "substantially equivalent" devices by claiming that they would be used in the long bones of the arms and legs when the company actually had intended to market them principally for use in spinal fusion surgery.<sup>375</sup>

The *Buckman* Court held that the plaintiffs' fraud-on-the-agency claims were impliedly preempted by the Medical Device Amendments.<sup>376</sup> According to the Court, a conflict exists between common-law tort claims like the plaintiffs' and the FDA's need to balance a number of competing regulatory objectives.<sup>377</sup> One such objective is to protect the integrity of the licensing process. Section 510(k)'s disclosure requirements help achieve this objective, as do the wide range of enforcement options available to the FDA to detect and punish fraudulent

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<sup>370</sup> For a discussion of the PMA procedure, see Sasha B. Rieders, Note, *State Law Tort Claims and the FDA: Proposing a Consumer-Oriented Prescription in Medical Device Cases*, 25 CARDOZO L. REV. 1159, 1167-71 (2004).

<sup>371</sup> It is not known whether any of these plaintiffs ultimately prevailed. However, one court stated, "No federal court has resolved this question in favor of the plaintiff's claim." *Bailey v. Johnson*, 48 F.3d 965, 967 (6th cir. 1995).

<sup>372</sup> *Kemp*, 231 F.3d 233-36 (holding that fraud-on-the-FDA claims are expressly preempted by the MDA); *Bone Screw I*, 159 F.3d at 823-25 (refusing to hold that such claims were preempted); *Reeves*, 44 F.3d at 302 (holding that such claims were preempted). For a discussion the FDA's marketing approval process under the MDA, see *supra* text accompanying notes 33-44.

<sup>373</sup> 531 U.S. 341 (2001).

<sup>374</sup> *Id.* at 343.

<sup>375</sup> *Id.* at 346.

<sup>376</sup> *Id.* at 348.

<sup>377</sup> *Id.*

applications.<sup>378</sup> However, the FDA also must ensure that its licensing process does not slow down the introduction of new medical products into the market or interfere with the judgment of health care professionals.<sup>379</sup> In particular, the Court observed that allowing fraud-on-the-FDA claims would discourage off-label uses because drug companies would be concerned with potential tort liability.<sup>380</sup> Finally, the Court emphasized that the claims involved were not ordinary tort claims, but instead were based entirely on noncompliance with FDA disclosure requirements.<sup>381</sup> The *Buckman* decision effectively shut down fraud-on-the-FDA claims. Enterprising plaintiffs' lawyers quickly shifted from this theory to a thinly disguised substitute known as negligence per se.

## 2. Violations of the FDCA as Negligence Per Se

Under the principle of negligence per se, a court relies upon a statute or administrative regulation to define the standard of care in a negligence action.<sup>382</sup> By successfully invoking negligence per se, the plaintiff establishes as a matter of law that the defendant's conduct was negligent so that the plaintiff need only prove causation and damages in order to prevail.<sup>383</sup> Plaintiffs have argued that manufacturers of pharmaceutical products and medical devices who violate the FDCA or FDA regulations are negligent and subject to civil liability under state negligence per se doctrines for any injuries that are proximately caused by such violations. In general, most courts have declined to embrace this application of negligence

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<sup>378</sup> *Buckman*, 531 U.S. at 348-49. Even the less rigorous premarket notification requirements under § 510(k) require applicants to provide the FDA with information about the device's design and function. *Id.* at 345-46.

<sup>379</sup> *Id.* at 349-50.

<sup>380</sup> *Id.* at 350.

<sup>381</sup> *Id.* at 352-53.

<sup>382</sup> Andrew E. Costa, *Negligence Per Se Theories in Pharmaceutical & Medical Device Litigation*, 57 ME. L. REV. 51, 54 (2005).

<sup>383</sup> *In re Orthopedic Bone Screw Prods. Liab. Litig. (Bone Screw II)*, 193 F.3d 781, 790 (3d Cir. 1999); *In re TMI*, 67 F.3d 1103, 1118 (3d Cir. 1995).

per se.<sup>384</sup> Other courts have rejected negligence per se claims because the plaintiff was unable to prove causation.<sup>385</sup>

*Talley v. Danek Medical, Inc.* reflects the reasoning of those courts that have refused to apply the doctrine of negligence per se to claims based on alleged violations of the FDCA.<sup>386</sup> In that case, medical device manufacturer Danek had secured FDA approval for the Dyna-Lok Device, a pedicle screw fixation device,<sup>387</sup> as a Class II device, which would not require premarket approval from the FDA,<sup>388</sup> although at that time such devices had been classified as Class III devices, which would require premarket approval through the PMA process before being marketed for pedicle screw fixation.<sup>389</sup> The plaintiff, Janet Talley, had undergone a number of unsuccessful back surgeries in which the Dyna-Lok Device was attached to the pedicles of her spine. Danek had not sought premarket approval for the Dyna-Lok Device at the time of Talley's operations.<sup>390</sup> After suffering injuries and complications from the surgeries, Talley sued Danek, maintaining that the company had deliberately marketed the Dyna-Lok Device for a use that had not been approved by the FDA in violation of the FDCA and that the company had therefore been negligent as a matter of law.<sup>391</sup> Unlike the fraud-on-the-FDA cases, in which the plaintiffs focused their allegations on an unauthorized presence of off-label uses in the market, Talley argued that it was the *promotion* of the Dyna-Lok Device for off-label uses, rather than its mere presence in the market, that had caused her injuries.<sup>392</sup> The lower court granted the defendant's motion

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<sup>384</sup> *Bone Screw II*, 193 F.3d at 792; *Talley v. Danek Med., Inc.*, 179 F.3d 154, 161 (4th Cir. 1999); *Sharp v. Artifex, Ltd.*, 110 F. Supp. 2d 388, 394-95 (W.D. Pa. 1999); *Baker v. Danek Medical*, 35 F. Supp. 2d 875, 878 (N.D. Fla. 1998); *King v. Danek Med., Inc.*, 37 S.W.3d 429, 460 (Tenn. Ct. App. 2000); *Cali v. Danek Med., Inc.*, 24 F. Supp. 2d 941, 954 (W.D. Wis. 1998). *But see* *Stanton v. Astra Pharm. Prods., Inc.*, 718 F.2d 553, 558-59 (3d Cir. 1983).

<sup>385</sup> *Menges v. Depuy Motech, Inc.*, 61 F. Supp. 2d 817, 829 (N.D. Ind. 1999); *Minisan v. Danek Med., Inc.*, 79 F. Supp. 2d 970, 975-77 (N.D. Ind. 1999); *Sita v. Danek Med., Inc.*, 43 F. Supp. 2d 245, 264-65 (E.D.N.Y. 1999); *Valente v. Sofamor, S.N.C.*, 48 F. Supp. 2d 862, 876-77 (E.D. Wis. 1999); *Baker v. Danek Medical, Inc.*, 35 F. Supp. 2d 875, 878 (N.D. Fla. 1998); *Osburn v. Danek Med., Inc.*, 520 S.E.2d 88, 94 (N.C. Ct. App. 1999); *Harden v. Danek Med., Inc.*, 985 S.W.2d 449, 453 (Tenn. Ct. App. 1998).

<sup>386</sup> *Talley*, 179 F.3d at 160-61.

<sup>387</sup> *See supra* note 366.

<sup>388</sup> *Talley*, 179 F.3d at 160.

<sup>389</sup> *Id.*

<sup>390</sup> *Id.*

<sup>391</sup> *Id.* at 160.

<sup>392</sup> *Id.*

for summary judgment, concluding that Talley had failed to show any evidence of negligence, and the plaintiff appealed.<sup>393</sup>

On appeal, the plaintiff in *Talley* renewed her claim that Danek had violated the FDCA by marketing a surgical device for a use that had not been approved by the FDA.<sup>394</sup> In particular, the plaintiff argued that “while purportedly selling the Dyna-Lok Device for its Class II purpose, Danek was in fact marketing the device for the unapproved Class III purpose of use in the pedicles of the spine . . . .”<sup>395</sup> According to the plaintiff, this alleged violation of the FDCA supported a claim based on negligence per se.<sup>396</sup> However, the court observed that the doctrine of negligence per se does not automatically create a private cause of action for every violation of a statute.<sup>397</sup> In the first place, not all statutory provisions establish a standard of care, and therefore not all statutory violations provide a basis for applying the doctrine of negligence per se.<sup>398</sup> In addition, even when a statute does establish a standard of care, the plaintiff must also prove the additional elements of negligence, including duty, causation, and injury.<sup>399</sup>

Addressing the standard of care issue, the court declared that violation of a statute that does not define a standard of care but merely imposes an administrative requirement will not support a negligence per se claim.<sup>400</sup> According to the court, licensing and reporting requirements, even when they are part of a regulatory scheme that is designed to protect public safety, are statutory requirements that do not establish a standard of care.<sup>401</sup> Applying this principle to the FDA’s licensing requirements, the court concluded that the general requirement that drugs and medical devices receive FDA approval before marketing was “only a tool to facilitate administration of the underlying regulatory scheme” and did not embody any substantive standard of care.<sup>402</sup> Consequently, even if Danek had failed to comply with the FDA’s licensing

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<sup>393</sup> *Talley v. Danek Med., Inc.*, 7 F. Supp. 2d 725 (E.D. Va. 1998).

<sup>394</sup> *Talley*, 179 F.3d at 160.

<sup>395</sup> *Id.*

<sup>396</sup> *Id.*

<sup>397</sup> *Id.* at 158.

<sup>398</sup> *Id.* at 159.

<sup>399</sup> *Id.*

<sup>400</sup> *Id.*

<sup>401</sup> *Id.*

<sup>402</sup> *Id.* at 161.

requirements, this by itself would not support a negligence per se claim.<sup>403</sup>

Moreover, as previously noted, the court held that even if the doctrine of negligence per se were applicable, the plaintiff would still be required to prove the other elements of a negligence claim.<sup>404</sup> In this case, the court determined that the plaintiff failed to present any evidence that Danek's failure to obtain proper FDA approval for the Dyna-Lok Device had caused her injuries.<sup>405</sup> Indeed, as the court pointed out, the FDA's subsequent approval of pedicle screw fixation devices as Class II devices suitable for spinal fusion surgery indicated that the agency thought that bone screw devices such as the defendant's product could be safely used for this purpose.<sup>406</sup> Nor was there any evidence that the plaintiff's doctor would have chosen some other device if he had known that the FDA had not approved the Dyna-Lok Device for spinal fusion surgery at the time of the plaintiff's operation.<sup>407</sup> Consequently, the court concluded that the plaintiff failed to establish that the defendant's alleged violation of the statute had proximately caused her injuries and therefore upheld the lower court's dismissal of her negligence per se claim.<sup>408</sup>

A Tennessee appeals court in *King v. Danek Medical, Inc.* agreed with the *Talley* court's reasoning.<sup>409</sup> Like *Talley*, *King* involved a negligence per se claim against the manufacturer of the TSRH device, a pedicle screw spinal fixation mechanism similar to Danek's Dyna-Lok device.<sup>410</sup> Danek had obtained an Investigational Device Exemption to conduct clinical trials on its TSRH Device.<sup>411</sup> However, according to the plaintiffs, while these clinical trials were going on, Danek had promoted the device for use in spinal pedicle surgery "[o]n a massive and perhaps unprecedented basis," thereby violating various provisions of the FDCA.<sup>412</sup> On appeal from the trial court's dismissal of their claim, the plaintiffs argued that marketing a surgical device that had not received premarket

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<sup>403</sup> *Id.*

<sup>404</sup> *Id.* at 158.

<sup>405</sup> *Id.* at 161.

<sup>406</sup> *Id.*

<sup>407</sup> *Id.*

<sup>408</sup> *Id.*

<sup>409</sup> *King v. Danek Med., Inc.*, 37 S.W.3d 429 (Tenn. Ct. App. 2000).

<sup>410</sup> *Id.* at 430.

<sup>411</sup> *Id.* at 455. See *supra* note 39 for an explanation of the IDE process.

<sup>412</sup> *Id.*

approval from the FDA violated the FDCA and constituted negligence per se.<sup>413</sup> Quoting *Talley*, the appellate court declared that the requirement of FDA approval prior to marketing is “only a tool to facilitate administration of the underlying regulatory scheme.”<sup>414</sup> Furthermore, because the approval requirement lacks any “independent substantive content,” it does not embody a standard of care.<sup>415</sup> The court concluded that breach of this requirement is akin to driving without a driver’s license and provides no basis for a negligence per se claim.<sup>416</sup> Consequently, the *King* court affirmed the lower court’s dismissal of the plaintiffs’ negligence per se claim.<sup>417</sup>

*In re Orthopedic Bone Screw Products Liability Litigation* presents an interesting variation on the negligence per se argument because the case involved conspiracy claims.<sup>418</sup> This multidistrict litigation involved more than 2000 lawsuits and approximately 5000 individual plaintiffs.<sup>419</sup> The plaintiffs alleged that several conspiracies existed on the part of bone screw manufacturers and others to promote their orthopedic bone screw products in violation of FDA regulations.<sup>420</sup>

The plaintiffs first claimed that individual bone screw manufacturers had agreed to give royalties and stock options to orthopedic surgeons and other physicians in return for their participation in seminars that were held apparently to inform physicians about the medical uses of bone screw devices.<sup>421</sup> According to the plaintiffs, the real purpose of these seminars was to promote the bone screw manufacturer’s products.<sup>422</sup> In addition, the physicians who conducted these seminars had failed to inform their audiences that the bone screw devices they were promoting had not received FDA approval for use in pedicle fixation surgery and that clinical trials had actually

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<sup>413</sup> *King*, 37 S.W.3d at 455.

<sup>414</sup> *Id.* at 457.

<sup>415</sup> *Id.*

<sup>416</sup> *Id.*

<sup>417</sup> *Id.* at 460.

<sup>418</sup> *Bone Screw II*, 193 F.3d 781 (3d Cir. 1999); see also *Cali v. Danek Med., Inc.*, 24 F. Supp. 2d 941, 947 (W.D. Wis. 1998) (alleging a conspiracy among bone screw manufacturers to promote an off-label use of their products). For a discussion of the use of civil conspiracy theories in products liability litigation, see Richard C. Ausness, *Conspiracy Theories: Is There a Place for Civil Conspiracy in Products Liability Litigation?*, 74 TENN. L. REV. 383 (2007).

<sup>419</sup> *Bone Screw II*, 193 F.3d at 784.

<sup>420</sup> *Id.* at 786-87.

<sup>421</sup> *Id.* at 786.

<sup>422</sup> *Id.*

raised serious concerns about the safety and effectiveness of bone screw devices when used in this manner.<sup>423</sup> Furthermore, seminar speakers had not disclosed that they had a financial interest in promoting this form of off-label use.<sup>424</sup>

The plaintiffs' second civil conspiracy claim alleged that bone screw device manufacturers had paid various professional associations to sponsor and present seminars for orthopedic surgeons in order to promote the use of bone screws in spinal fixation surgery.<sup>425</sup> As in the previous conspiracy claim, the plaintiffs declared that the conspirators had concealed that the FDA had not approved the use of bone screws in pedicle fixation surgery, that studies had revealed problems with this procedure, and that the professional associations had been paid to promote the off-label use of these devices.<sup>426</sup> The plaintiffs also claimed that a trade association established by the conspirators had conducted a fraudulent study to use in civil litigation and that certain conspirators, in order to obtain § 510(k) clearance for their products as substantially equivalent devices, had falsely told the FDA that one company had marketed a bone screw device for pedicle fixation surgery prior to 1976.<sup>427</sup>

The lower court dismissed these claims, holding that an independent basis of liability was necessary to bring a civil conspiracy claim and that violation of the FDCA did not satisfy this requirement.<sup>428</sup> On appeal, the Third Circuit observed that there is no private right of action for violations of the FDCA.<sup>429</sup> The court also agreed with the lower court's conclusion that one cannot sue a group of defendants for conspiring to engage in conduct that would not be actionable against an individual defendant.<sup>430</sup> Because the plaintiffs could not sue individual defendants for violations of the FDCA, they could not sue them for conspiring to engage in conduct that violates the FDCA either.<sup>431</sup>

The plaintiffs also argued that violations of federal statutes could be the basis of common law liability under the

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<sup>423</sup> *Id.* at 786-87.

<sup>424</sup> *Id.* at 787.

<sup>425</sup> *Id.*

<sup>426</sup> *Id.*

<sup>427</sup> *Id.*

<sup>428</sup> *Id.*

<sup>429</sup> *Id.* at 789-90.

<sup>430</sup> *Id.*

<sup>431</sup> *Id.*

principle of negligence per se and thereby provide the underlying tort necessary to support a civil conspiracy claim.<sup>432</sup> The appeals court, however, responded that negligence per se did not create an independent basis of tort liability, but merely established a standard of care for an underlying tort.<sup>433</sup> In the court's view, the plaintiffs' bootstrapping interpretation of negligence per se "would allow private plaintiffs to recover for violations of a federal statute that creates no private cause of action and, in fact, expressly restricts its enforcement to the federal government."<sup>434</sup> If the plaintiffs were allowed to prevail, they could sidestep the FDCA's prohibition against private enforcement actions merely by bringing a civil conspiracy action instead of suing defendants for individual actions.<sup>435</sup> For this reason, the court concluded that the plaintiffs' conspiracy claims were properly dismissed.<sup>436</sup>

As mentioned earlier, a number of courts have also rejected negligence per se claims on causation grounds.<sup>437</sup> *Menges v. Depuy Motech, Inc.* is illustrative of this approach.<sup>438</sup> This case also involved the marketing of orthopedic bone screw devices for use in spinal fusion therapy.<sup>439</sup> The plaintiff alleged that, because the pedicle screw device did not have FDA approval for implantation into the vertebral pedicle, Depuy Motech was prohibited from marketing it for use in spinal fixation surgery and had a duty to regulate the use of its devices in hospitals.<sup>440</sup> According to the plaintiff, the defendant's violation of FDA regulations constituted negligence per se.<sup>441</sup> In response to a motion for summary judgment by the defendant, the court acknowledged that Wisconsin law would permit the plaintiff to base his negligence per se claim on violation of the FDCA.<sup>442</sup> However, the court ultimately granted the defendant's summary judgment motion, finding that the plaintiff had not produced any medical evidence that his

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<sup>432</sup> *Bone Screw II*, 193 F.3d at 790.

<sup>433</sup> *Id.*

<sup>434</sup> *Id.* at 791.

<sup>435</sup> *Id.*

<sup>436</sup> *Id.* at 792.

<sup>437</sup> See *supra* note 385 and accompanying text.

<sup>438</sup> *Menges v. Depuy Motech, Inc.*, 61 F. Supp. 2d 817 (N.D. Ind. 1999).

<sup>439</sup> *Id.* at 820.

<sup>440</sup> *Id.* at 823.

<sup>441</sup> *Id.* at 829.

<sup>442</sup> *Id.* (citing *Valente v. Sofamor, S.N.C.*, 48 F. Supp. 2d 862, 876 (E.D. Wis. 1999)).

doctor's use of the defendant's device was a proximate cause of his injury.<sup>443</sup>

### B. *Fraudulent Misrepresentation*

In addition to basing tort claims on violations of the FDCA, injured consumers have also sued drug and medical device manufacturers for fraudulent misrepresentation.<sup>444</sup> A fraudulent misrepresentation claim requires proof by clear and convincing evidence of the following elements:

- (1) a representation;
- (2) which is material to the transaction at hand;
- (3) made falsely, with knowledge of its falsity or recklessness as to whether it is true or false;
- (4) with the intent of misleading another into relying on it;
- (5) justifiable reliance on the misrepresentation;
- and (6) the resulting injury was proximately caused by the reliance.<sup>445</sup>

Fraudulent misrepresentation claims in this area have often failed because plaintiffs were unable to establish either reliance or causation.<sup>446</sup>

*Miller v. Pfizer Inc. (Roerig Division)* is illustrative of the difficulties plaintiffs face when they base their claim on fraudulent misrepresentation.<sup>447</sup> The plaintiffs in *Miller* sued Pfizer in federal court after its anti-depression drug, Zoloft, allegedly caused their thirteen-year-old son, Matthew, to commit suicide.<sup>448</sup> The plaintiffs sought to hold Pfizer strictly liable for marketing defects and misrepresentations about Zoloft.<sup>449</sup> Pfizer moved for partial summary judgment on the defective marketing and failure-to-warn claims.<sup>450</sup>

<sup>443</sup> *Id.*

<sup>444</sup> See, e.g., *McCauley v. Purdue Pharma L.P.*, 331 F. Supp. 2d 449, 461 (W.D. Va. 2004) (*OxyContin*); *Wethington v. Purdue Pharma L.P.*, 218 F.R.D. 577, 582 (S.D. Ohio 2003) (*OxyContin*); *Osburn v. Danek Med., Inc.*, 520 S.E.2d 88, 95 (N.C. Ct. App. 1999) (spinal fixation device); *Harden v. Danek Med., Inc.*, 985 S.W.2d 449, 453 (Tenn. Ct. App. 1998) (spinal fixation device).

<sup>445</sup> *Ausness*, *supra* note 418, at 400 (quoting *Goldstein v. Philip Morris, Inc.*, 854 A.2d 585, 590-91 (Pa. Super. Ct. 2004)).

<sup>446</sup> *Talley v. Danek Med., Inc.*, 179 F.3d 154, 161 (4th Cir. 1999); *McCauley*, 331 F. Supp. 2d at 462; *Sita v. Danek Med., Inc.*, 43 F. Supp. 2d 245, 260 (E.D.N.Y. 1999); *Baker v. Danek Med.*, 35 F. Supp. 2d 875, 878 (N.D. Fla. 1998); *Osburn*, 520 S.E.2d at 95; *Harden*, 985 S.W.2d at 453.

<sup>447</sup> *Miller v. Pfizer Inc. (Roerig Div.)*, 196 F. Supp. 2d 1095 (D. Kan. 2002).

<sup>448</sup> *Id.* at 1097.

<sup>449</sup> *Id.* In addition, the complaint set forth a negligence claim based on the defendant's failure to test and warn about the risk of drug-induced suicide when Zoloft was prescribed off-label for children. *Id.*

<sup>450</sup> *Id.*

With respect to their “defective marketing claim,” the plaintiffs contended that Pfizer had “gone to great lengths to reassure doctors that the violence and suicide problems that they ha[d] heard about, mainly with its chief SSRI competitor Prozac, would not occur with Zoloft, and to assuage patient’s [sic] concerns over the initial adverse effects which are frequently the harbingers of tragedy . . . .”<sup>451</sup> As evidence of this marketing scheme, the plaintiffs relied on statements made by a Pfizer employee, James Lee Jung.<sup>452</sup> Mr. Jung had told the defendant’s professional medical representatives not to mention the risk of suicide from Zoloft to physicians unless they specifically asked about it.<sup>453</sup> In addition, Jung had told the representatives that if they were asked about suicide risk, they should assure physicians that Zoloft had a low risk of suicide ideation.<sup>454</sup>

Since the plaintiffs did not set forth any specific legal basis for their marketing defect claim, the court chose to characterize it as a fraud or misrepresentation claim.<sup>455</sup> The court pointed out that to sustain such a claim, plaintiffs must prove, *inter alia*, that they “reasonably relied and acted on the [defendant’s] allegedly false representations to their detriment.”<sup>456</sup> There apparently was no evidence that the plaintiffs had relied on any representations made by Pfizer; instead, the court concluded, “In allowing Matthew to use Zoloft, plaintiffs relied solely on Dr. Geenens’s [Matthew’s physician] advice.”<sup>457</sup>

According to Pfizer, even if the plaintiffs could show reliance on their part, the learned intermediary doctrine required them to prove that Dr. Geenens had relied on marketing materials or other information about Zoloft that Pfizer had provided him.<sup>458</sup> Unfortunately for the plaintiffs, Dr. Geenens steadfastly maintained that his decision to prescribe Zoloft to treat Matthew’s depression had not been influenced by

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<sup>451</sup> *Id.* at 1119 (internal quotation marks and citation omitted).

<sup>452</sup> *Id.* at 1100 n.7.

<sup>453</sup> *Id.*

<sup>454</sup> *Id.*

<sup>455</sup> *Id.* at 1119.

<sup>456</sup> *Id.*

<sup>457</sup> *Id.* at 1099.

<sup>458</sup> *Id.* at 1120. The learned intermediary doctrine provides that a manufacturer satisfies its duty to warn about a prescription drug’s inherent risks without warning the patient directly when it adequately warns the prescribing physician. *See infra* text accompanying notes 513-517.

Pfizer's advertising or promotional materials.<sup>459</sup> Furthermore, Dr. Geenens testified that Pfizer's sales representatives had never encouraged him to prescribe Zoloft for any off-label uses.<sup>460</sup> In response, the plaintiffs argued that the Kansas Supreme Court, in *Hurlbut v. Conoco, Inc.*,<sup>461</sup> had eliminated the reliance requirement in misrepresentation cases involving products.<sup>462</sup> However the court rejected their interpretation of *Hurlbut*.<sup>463</sup> The plaintiffs also urged the court to adopt the position stated in Section 9 of the *Restatement (Third) of Torts: Products Liability*,<sup>464</sup> which would impose liability on product manufacturers for even innocent misrepresentations of material facts.<sup>465</sup> The court noted that even under Section 9 of the *Restatement*, proof of causation is required and if the plaintiffs could not establish reliance, they could not establish causation either.<sup>466</sup> The plaintiffs also asked the court to reject the learned intermediary doctrine, thereby relieving them of the burden of proving reliance on Dr. Geenens's part.<sup>467</sup> However, the court concluded that there was no evidence to show that Kansas courts had rejected the learned intermediary doctrine or were about to do so.<sup>468</sup>

The plaintiffs' final argument was that Pfizer's marketing campaign for Zoloft relied on subtle and subliminal techniques to persuade physicians like Dr. Geenens to prescribe Zoloft. The plaintiffs maintained that Dr. Geenens could have been influenced by these subliminal messages to prescribe Zoloft to Matthew.<sup>469</sup> According to this argument, the reliance requirement for misrepresentation would be satisfied even though Dr. Geenens denied that he had relied on any representations about the safety of Zoloft provided by Pfizer. However, the court ultimately concluded that even if Pfizer had employed subliminal advertising techniques, the plaintiffs failed to show that they had any effect on Dr. Geenens's

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<sup>459</sup> *Miller*, 196 F. Supp. 2d at 1100.

<sup>460</sup> *Id.*

<sup>461</sup> 856 P.2d 1313, 1320 (Kan. 1993).

<sup>462</sup> *Miller*, 196 F. Supp. 2d at 1120.

<sup>463</sup> *Id.*

<sup>464</sup> RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIAB. § 9 (1998).

<sup>465</sup> *Miller*, 196 F. Supp. 2d at 1120.

<sup>466</sup> *Id.* at 1121.

<sup>467</sup> *Id.*

<sup>468</sup> *Id.* at 1122.

<sup>469</sup> *Id.*

decision to prescribe Zoloft to their son.<sup>470</sup> Consequently, the court granted the defendant's request for summary judgment on the marketing defect and misrepresentation claims.<sup>471</sup>

Thus, as *Miller* illustrates, although misrepresentation claims are available in theory to plaintiffs seeking recovery from pharmaceutical companies that promote off-label uses, in reality this cause of action does not pose a serious threat to drug manufacturers because of the difficulties in making out a case.

### C. *Failure to Warn*

Product sellers, including manufacturers of drugs and medical devices, have a duty to warn about the inherent risks associated with the use of their products when the risks may not be obvious to consumers. Some cases are concerned with whether a manufacturer must warn about risks that are unique to particular off-label uses of the product. Another group of cases have considered what role the learned intermediary rule plays when a product is used for an off-label purpose.

#### 1. Failure to Warn About Risks Associated with Particular Off-Label Uses

A manufacturer has a duty to provide an adequate warning of any danger inherent in the normal use of its product that is not likely to be within the knowledge of the ordinary user.<sup>472</sup> In some cases, this duty may require a drug manufacturer to warn physicians about the risks of particular off-label uses. For example, in *Knowlton v. Deseret Medical, Inc.*, the manufacturer of a catheter and needle placement unit known as Intracath was held liable for chemical burns suffered by the plaintiff during open-heart surgery.<sup>473</sup> The plaintiff's surgery involved a procedure known as retrograde threading, in which two small hollow flexible tubes, or catheters, are inserted into the left and right atria of the heart.<sup>474</sup> The

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<sup>470</sup> *Id.* at 1122-23.

<sup>471</sup> *Id.* at 1123.

<sup>472</sup> *See, e.g.,* Winterrowd v. Travelers Indem. Co., 462 So. 2d 639, 642 (La. 1985); Hebert v. Brazzel, 403 So. 2d 1242, 1245 (La. 1981).

<sup>473</sup> *Knowlton v. Deseret Med., Inc.*, 930 F.2d 116, 117 (1st Cir. 1991).

<sup>474</sup> *Id.* Retrograde threading involves the insertion of one end of a catheter into the right atrium and the threading of the other end into a hollow needle with

catheter in *Knowlton* was used to transmit the drug Nitroprusside (Nipride) to the patient's heart.<sup>475</sup> Some of the Nipride solution leaked from a cut or hole in the catheter into the plaintiff's chest and abdominal walls, causing severe chemical burns.<sup>476</sup>

At trial, the jury found that the manufacturer had failed to adequately warn physicians of the danger inherent in the use of the Intracath device.<sup>477</sup> On appeal, the First Circuit Court of Appeals observed that the Intracath device was intended for use in venipunctures—the insertion of the needle and catheter into a vein.<sup>478</sup> However, there was testimony that the manufacturer had been aware that the use of its catheters and needles as atrial lines during open-heart surgery was a common off-label procedure.<sup>479</sup> Furthermore, company officials had acknowledged that they knew there was a significant risk that the catheter tube might be cut or nicked by the needle if retrograde threading were employed.<sup>480</sup> The appeals court also noted that a cut or nick sufficient to create a hole in the catheter would be invisible to the naked eye and, thus, unlikely to be discovered by the operating surgeon.<sup>481</sup> Finally, the court found that a warning was appropriate because a reasonably prudent heart surgeon would not be aware of the danger inherent in the retrograde threading procedure.<sup>482</sup> Consequently, the court concluded that the jury verdict was correct and upheld the plaintiff's failure-to-warn claim against the defendant.<sup>483</sup>

An Illinois appellate court reached a similar result in *Proctor v. Davis*.<sup>484</sup> *Proctor* concerned the Upjohn Company's 1959 FDA approval to market the anti-inflammatory drug Depo-Medrol for intramuscular (in the muscle), intra-articular (in the joint), and intralesional (in a lesion) injections.<sup>485</sup> Depo-

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sharp beveled edges that is inserted into the chest wall. *Id.* at 118. The needle and catheter are then pulled back through the chest wall and the needle removed so that the catheter can be used as a drug delivery device. *Id.*

<sup>475</sup> *Id.*

<sup>476</sup> *Id.*

<sup>477</sup> *Id.* at 118-19.

<sup>478</sup> *Id.* at 119.

<sup>479</sup> *Id.*

<sup>480</sup> *Id.*

<sup>481</sup> *Id.* at 122.

<sup>482</sup> *Id.*

<sup>483</sup> *Id.* at 122-23.

<sup>484</sup> 682 N.E.2d 1203, 1215 (Ill. Ct. App. 1997).

<sup>485</sup> *Id.* at 1206.

Medrol was a sterile, aqueous suspension containing methyl prednisone acetate, a corticosteroid, and was useful in treating various inflammatory bodily disorders.<sup>486</sup> Depo-Medrol was an insoluble toxic material that was intended to be released in the patient's body over a period of six to eight weeks and ultimately carried away in the bloodstream.<sup>487</sup>

Shortly after the FDA approved the drug, two ophthalmologists independently contacted Upjohn about using Depo-Medrol clinically to treat ophthalmic conditions by means of periocular (near the eye) injections. Upjohn encouraged the doctors and provided them with a supply of the drug for their proposed use, but failed to inform them that no animal studies had been performed to test the drug's effect on periocular tissue.<sup>488</sup> Subsequently, in the early 1960s, Upjohn also provided financial support to doctors who used Depo-Medrol for unapproved subconjunctival injections.<sup>489</sup> Furthermore, the drug company also distributed an article about off-label uses of the drug, but failed to provide information about "unsatisfactory" animal experiments that the author had conducted.<sup>490</sup> As periocular injection of Depo-Medrol became increasingly popular,<sup>491</sup> partly due to Upjohn's marketing efforts, the company considered submitting a supplemental New Drug Application for this use to the FDA, but decided not to do so.<sup>492</sup> In fact, periocular injection of Depo-Medrol was quite risky because if the physician inadvertently injected the drug into the patient's eye, it would remain in the eye for a long time and cause serious injury because the eye does not possess a blood supply to enable it to remove the drug.<sup>493</sup> Moreover, because Depo-Medrol was insoluble, it increased pressure within the eye and caused other damage.<sup>494</sup>

In 1983, the plaintiff's physician, Dr. Davis, began a program of periocular injections of Depo-Medrol to treat vision problems associated with cystoid macular edema.<sup>495</sup> During one of these treatments, Dr. Davis mistakenly injected Depo-

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<sup>486</sup> *Proctor*, 682 N.E.2d at 1206.

<sup>487</sup> *Id.*

<sup>488</sup> *Id.*

<sup>489</sup> *Id.* at 1207.

<sup>490</sup> *Id.*

<sup>491</sup> *Id.* at 1212.

<sup>492</sup> *Id.* at 1209.

<sup>493</sup> *Id.* at 1206.

<sup>494</sup> *Id.*

<sup>495</sup> *Id.* at 1210.

Medrol directly into the plaintiff's left eye.<sup>496</sup> Despite a series of subsequent operations to remove the drug and repair the damage to his left eye, the plaintiff eventually lost all vision in the eye and his physicians were forced to remove it.<sup>497</sup> The plaintiff filed suit in 1984 against Dr. Davis and Upjohn, alleging malpractice against the doctor and claiming that Upjohn had failed to warn doctors about the dangers of using Depo-Medrol for off-label periocular injection.<sup>498</sup> The jury found in favor of Dr. Davis, but subjected Upjohn to liability for compensatory and punitive damages.<sup>499</sup>

On appeal, the Illinois appellate court declared that a drug manufacturer has a continuing duty to warn of product-related risks that are not generally known to the medical community.<sup>500</sup> According to the court, when the manufacturer of a potentially harmful product possesses information not generally known to prescribing physicians, it has a duty to share this information with them by means of warnings.<sup>501</sup> In this case, the record showed that at the time of the operation Upjohn was aware of the risks associated with periocular injection of Depo-Medrol and was also aware that many ophthalmologists were administering the drug in this fashion as an off-label use.<sup>502</sup> Consequently, Upjohn had a legal obligation to warn about the risks of periocular injection of Depo-Medrol, and its failure to do so made the drug defective and unreasonably dangerous.<sup>503</sup>

*Knowlton* and *Proctor* suggest that most courts will probably uphold failure-to-warn claims if the risks associated with a particular off-label use is serious, the use is common or widespread, and if the manufacturer knows of the off-label use or has encouraged it.<sup>504</sup> On the other hand, drug companies ordinarily have no duty to warn of off-label uses that are unforeseeable. In *Rhoto v. Ribando*, a self-proclaimed weight reduction specialist prescribed a regime of prescription medications, along with a conservative diet plan, to help the

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<sup>496</sup> *Id.* at 1210.

<sup>497</sup> *Id.* at 1211.

<sup>498</sup> *Id.*

<sup>499</sup> *Id.*

<sup>500</sup> *Id.*

<sup>501</sup> *Id.* at 1213-14.

<sup>502</sup> *Id.* at 1212.

<sup>503</sup> *Id.* at 1213.

<sup>504</sup> Noah, *supra* note 7, at 161-62.

plaintiff lose weight.<sup>505</sup> After following this weight-loss program for two weeks, the plaintiff suffered a massive stroke.<sup>506</sup> In her suit against the drug manufacturers, the plaintiff argued that they had failed to warn of the danger of a stroke when various drugs were used individually or in combination with other drugs prescribed in connection with her weight reduction program.<sup>507</sup> At the conclusion of the trial, the court directed a verdict for the defendants on the ground that the plaintiff's doctor grossly misused the drugs.<sup>508</sup>

On appeal, the plaintiff contended that the warnings for the individual drugs were inadequate because they did not warn about the dangers associated with using them in weight control programs, a practice that the manufacturers knew or should have known was taking place.<sup>509</sup> The court, however, observed that all of the expert witnesses at trial testified that the prescription of the particular combination of drugs used in the plaintiff's diet plan was a gross misuse of the products.<sup>510</sup> The court declared that a manufacturer is only required to warn of dangers associated with the normal use of its product and concluded that the warnings provided by the drug manufacturers in this case satisfied this requirement.<sup>511</sup> Consequently, it affirmed the lower court's decision in favor of the defendants.<sup>512</sup>

## 2. The Learned Intermediary Doctrine as a Defense to Failure-to-Warn Claims

The learned intermediary rule is a substantial barrier to recovery for plaintiffs who bring failure-to-warn claims. As noted above, as a general rule, manufacturers have a duty to warn the ultimate users or consumers of their products about the inherent risks of those products when the risks may not be obvious. However, an exception to the general rule, known as the "learned intermediary doctrine," applies to prescription

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<sup>505</sup> *Rhoto v. Ribando*, 504 So. 2d 1119, 1120 (La. Ct. App. 1987).

<sup>506</sup> *Id.*

<sup>507</sup> *Id.* at 1121.

<sup>508</sup> *Id.*

<sup>509</sup> *Id.* at 1123-24.

<sup>510</sup> *Id.* at 1124.

<sup>511</sup> *Id.* at 1124-26.

<sup>512</sup> *Id.* at 1126.

drugs and medical devices.<sup>513</sup> The learned intermediary rule provides that the manufacturer of a prescription drug or medical device is only required to warn a patient's prescribing physician and does not have to warn the patient directly.<sup>514</sup> This rule gets its name from the fact that the physician is expected to act as an informed intermediary between the manufacturer and the patient.<sup>515</sup> Thus, the manufacturer may be held liable for injuries caused by the defective prescription of a product if the manufacturer fails to provide an effective warning to the prescribing physician.<sup>516</sup> On the other hand, if a manufacturer provides an adequate warning to the prescribing physician, the manufacturer is not subject to liability, and the physician has a duty to pass this information on to the patient.<sup>517</sup> However, a plaintiff cannot prevail on a failure-to-warn theory against a manufacturer even when the defendant's warning is inadequate if the learned intermediary (the physician) was already aware of the risk at the time of prescription. In effect, the defendant's failure to warn is not regarded as a cause-in-fact of the plaintiff's injury. Drug manufacturers have often successfully invoked this principle in off-label use cases.

*Sita v. Danek Medical, Inc.* illustrates this principle. In that case, a plaintiff who underwent spinal fixation surgery sustained injuries when the defendant's bone screw device, the TSRH System, fractured.<sup>518</sup> In a suit against the manufacturer, the plaintiff alleged, inter alia, that the warnings in the product's package insert had not been adequate.<sup>519</sup> The plaintiff contended that although the package insert had warned about such risks as pseudarthrosis, breakage, neurological impairment, and pain, it should have also disclosed that the TSRH

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<sup>513</sup> See Yonni D. Fushman, Comment, *Perez v. Wyeth Labs., Inc.: Toward Creating a Direct-to-Consumer Advertisement Exception to the Learned Intermediary Doctrine*, 80 B.U. L. REV. 1161, 1162 (2000).

<sup>514</sup> Richard C. Ausness, *Will More Aggressive Marketing Practices Lead to Greater Tort Liability for Prescription Drug Manufacturers?*, 37 WAKE FOREST L. REV. 97, 106-07 (2002).

<sup>515</sup> *Reaves v. Ortho Pharm. Corp.*, 765 F. Supp. 1287, 1289 (E.D. Mich. 1991); *Martin v. Hacker*, 628 N.E.2d 1308, 1311 (N.Y. 1993).

<sup>516</sup> See *Mahr v. G.D. Searle & Co.*, 390 N.E.2d 1214, 1228 (Ill. Ct. App. 1979).

<sup>517</sup> See *Brooks v. Medtronic, Inc.*, 750 F.2d 1227, 1232 (4th Cir. 1984). This is an aspect of a physician's obligation to inform patients of the risks associated with a particular treatment under the doctrine of informed consent. See generally Peter H. Schuck, *Rethinking Informed Consent*, 103 YALE L.J. 899 (1994).

<sup>518</sup> *Sita v. Danek Med., Inc.*, 43 F. Supp. 2d 245, 250 (E.D.N.Y. 1999).

<sup>519</sup> *Id.* at 259.

Device had not been approved for pedicle implantation.<sup>520</sup> According to the plaintiff,

due to the boiler-plate nature of the language used and the warning's failure to state that certain components of the TSRH System had not been approved for use in pedicle surgery, these warnings, taken alone, might not fully apprise a doctor of the risks associated with the use of TSRH components.<sup>521</sup>

However, the court rejected this argument, pointing out that the package insert had expressly stated that the TSRH System's components were intended for "attachment to the sacrum or ilium only."<sup>522</sup> In the court's opinion, this language was sufficient to inform an experienced doctor, such as the plaintiff's physician, that the TSRH screws had not been approved for use in the pedicles.<sup>523</sup> Accordingly, the court granted the defendant's motion for summary judgment on the failure-to-warn claim.<sup>524</sup>

### 3. Overpromotion as a Defense to Adequate Warnings

An otherwise satisfactory warning may be deemed to be inadequate in a failure-to-warn case because the manufacturer diluted the effect of the warning by "overpromotion."<sup>525</sup> For example, assurances of safety by a drug company's sales representatives may negate FDA-approved warnings contained in product labeling or the Physician's Desk Reference.<sup>526</sup>

Courts appear to be split on the question of whether a plaintiff can maintain an overpromotion claim when the physician is aware of the risk that has been diluted by the manufacturer's overpromotion. *Love v. Wolf*<sup>527</sup> and *Formella v. Ciba-Geigy Corp.*<sup>528</sup> represent differing views on this issue. *Love* involved Cholormycetin, a wide-spectrum antibiotic manufactured by Parke-Davis<sup>529</sup> that was widely prescribed for off-label

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<sup>520</sup> *Id.*

<sup>521</sup> *Id.*

<sup>522</sup> *Id.* at 259-60.

<sup>523</sup> *Id.* at 260.

<sup>524</sup> *Id.*

<sup>525</sup> David G. Owen et al., *in* 2 DAVID G. OWEN ET AL., MADDEN & OWEN ON PRODUCTS LIABILITY § 22:8, at 565-66 (3d ed. 2000).

<sup>526</sup> *See, e.g.,* Incollingo v. Ewing, 282 A.2d 206, 284 (Pa. 1971), *abrogated on other grounds by* Kaczkowski v. Bolubasz, 421 A.2d 1027 (Pa. Sept. 1980).

<sup>527</sup> 38 Cal. Rptr. 183 (Ct. App. 1964).

<sup>528</sup> 300 N.W.2d 356 (Mich. Ct. App. 1980).

<sup>529</sup> *Love*, 38 Cal. Rptr. at 184.

uses during the 1970s.<sup>530</sup> The plaintiff suffered severe aplastic anemia after her doctor prescribed Cholormycetin to treat a gum infection.<sup>531</sup> At the time of the plaintiff's injury, Cholormycetin's package labeling warned of the risk of aplastic anemia and other blood dyscrasias and cautioned that the drug "should not be used indiscriminately or for minor infections."<sup>532</sup> The labeling also declared that adequate blood studies should be made when Cholormycetin was prescribed for intermittent or prolonged use.<sup>533</sup>

The plaintiff's physician, Dr. Wolf, prescribed a total of ninety-six Cholormycetin capsules during a relatively short time to treat a gum infection and bronchitis, but failed to perform any blood tests.<sup>534</sup> At the trial, Dr. Wolf admitted that these conditions were not sufficiently dangerous to fall within the types of infections that Cholormycetin was intended to treat.<sup>535</sup> The jury apparently believed that the plaintiff's injuries were caused by Dr. Wolf's off-label prescription of the drug and found in favor of the plaintiff.<sup>536</sup>

On appeal, the court acknowledged that Parke-Davis had warned about the risk of aplastic anemia and had urged physicians to perform blood tests when Cholormycetin was prescribed on a long-term basis.<sup>537</sup> The court then turned to the plaintiff's argument that "such warnings must be deemed cancelled out if overpromotion through a vigorous sales program persuaded doctors to disregard the warnings given."<sup>538</sup> The court described how the Parke-Davis sales representatives had encouraged off-label use of the drug by downplaying the risk of aplastic anemia and falsely informing physicians that the FDA had approved Cholormycetin "with no restrictions on the number or range of diseases for which Cholormycetin may be administered."<sup>539</sup> The court also observed that sales of Cholormycetin were so numerous that it was apparent that

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<sup>530</sup> Christopher, *supra* note 13, at 249.

<sup>531</sup> *Love*, 38 Cal. Rptr. at 184. According to the court, aplastic anemia is a form of blood dyscrasia, a "condition resulting from the depression or destruction of the blood-forming elements in the bone marrow." *Id.* at 185.

<sup>532</sup> *Id.*

<sup>533</sup> *Id.*

<sup>534</sup> *Id.* at 186.

<sup>535</sup> *Id.* at 196.

<sup>536</sup> *Id.* at 184.

<sup>537</sup> *Id.* at 193.

<sup>538</sup> *Id.*

<sup>539</sup> *Id.* at 195.

the product was being prescribed for non-approved uses.<sup>540</sup> Although the court reversed the verdict because of misconduct on the part of the plaintiff's lawyer, it refused to dismiss the case against the drug company and instead ordered a new trial on the overpromotion issue.<sup>541</sup>

However, at least one legal commentator has criticized the court's reasoning in *Love*.<sup>542</sup> As Jonathan Grant pointed out, notwithstanding the defendant's promotional efforts, Dr. Wolf was fully aware of the risks of long-term use of Cholormycetin, yet chose to prescribe it anyway.<sup>543</sup> In Dr. Wolf's case, Parke-Davis's overpromotion did not vitiate the warnings that it provided on the drug's labeling and, therefore, did not cause the plaintiff's injuries.<sup>544</sup> In other words, Dr. Wolf's negligence—if his prescription of Cholormycetin was negligent—was the legal cause of the plaintiff's injury, not overpromotion of the drug by Parke-Davis.<sup>545</sup>

A Michigan appellate court reached a different conclusion from that in *Love* in *Formella v. Ciba-Geigy Corp.*<sup>546</sup> The plaintiff in that case developed aplastic anemia as a result of taking Tandearil, a drug manufactured by the defendant.<sup>547</sup> The plaintiff brought suit, claiming that the drug company Ciba-Geigy overpromoted Tandearil and failed to adequately warn her doctor about the risk of developing blood dyscrasia.<sup>548</sup> At the end of the trial, the lower court granted the Ciba-Geigy's motion for a directed verdict.<sup>549</sup> On appeal, the plaintiff contended that the trial court should not have excluded evidence of Ciba-Geigy's marketing plans.<sup>550</sup> The appeals court observed that the drug's package insert had indicated that the drug was contraindicated for patients, like the plaintiff, who were allergic to penicillin.<sup>551</sup> The package insert also had cautioned against treating persons over age sixty with Tandearil for more

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<sup>540</sup> *Id.*

<sup>541</sup> *Id.* at 197.

<sup>542</sup> Jonathan E. Grant, *The "Misuse" Defense in Drug Products Liability Cases*, 8 PACE L. REV. 535, 553 (1988).

<sup>543</sup> *Id.*

<sup>544</sup> *Id.*

<sup>545</sup> *Id.*

<sup>546</sup> 300 N.W.2d 356 (Mich. Ct. App. 1980).

<sup>547</sup> *Id.* at 357.

<sup>548</sup> *Id.*

<sup>549</sup> *Id.*

<sup>550</sup> *Id.*

<sup>551</sup> *Id.* at 359.

than a week.<sup>552</sup> In this case, the plaintiff was over sixty and her doctor had treated her with the drug for lower back pain (an off-label use) for more than six weeks.<sup>553</sup> Finally, the package insert had also recommended that blood tests be performed weekly for elderly patients taking Tandearil. The plaintiff's doctor had not performed any blood tests until she developed symptoms of aplastic anemia.<sup>554</sup>

The court concluded that the plaintiff's doctor had been aware that taking Tandearil for any length of time could cause blood dyscrasia and had ignored this risk.<sup>555</sup> According to the court, even if the drug company was guilty of overpromoting Tandearil, thereby diluting the effectiveness of the warnings, overpromotion was not the proximate cause of the plaintiff's injury.<sup>556</sup> Rather, the decision of the plaintiff's doctor to adopt a treatment regime that he knew would greatly increase the risk of blood dyscrasia had been an independent cause—and the sole proximate cause—of her injury.<sup>557</sup> Accordingly, the court affirmed the lower court's judgment in favor of Ciba-Geigy.<sup>558</sup> The court's approach in *Formella* seems to represent the prevailing view on the overpromotion issue in failure-to-warn cases.<sup>559</sup>

In general, failure to warn is a potential source of liability for drug manufacturers. In particular, manufacturers who promote off-label uses may be held liable for failing to warn doctors about the risks associated with a known off-label use. Moreover, even when manufacturers do provide warnings, a court may treat the warnings as inadequate if the manufacturer dilutes their effectiveness by overpromotion.

#### D. *The Duty to Test for Off-Label Related Risks*

Manufacturers are unlikely to test off-label uses of their products unless the FDA orders them to do so or they intend to file a supplemental NDA because clinical trials and other forms of testing can be expensive. Moreover, the failure to test for risks associated with particular off-label uses ordinarily does

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<sup>552</sup> *Id.*

<sup>553</sup> *Id.* at 357.

<sup>554</sup> *Id.*

<sup>555</sup> *Id.* at 358.

<sup>556</sup> *Id.*

<sup>557</sup> *Id.*

<sup>558</sup> *Id.* at 359.

<sup>559</sup> Grant, *supra* note 542, at 554.

not constitute negligence or make the product defective or unreasonably dangerous. However, at least one court has imposed liability for failure to test.<sup>560</sup>

In that decision—*Medics Pharmaceutical Corp. v. Newman*—the plaintiff was stricken with clear cell adenocarcinoma as a result of her mother's ingestion of DES.<sup>561</sup> The plaintiff's mother during her pregnancy had taken Diastyl, a brand of DES marketed, but not manufactured, by the defendant in order to prevent miscarriage.<sup>562</sup> The defendant claimed that it had not promoted Diastyl for use in preventing miscarriages and that the drug's package labeling had not mentioned this as an indicated use.<sup>563</sup> However, physicians had been commonly prescribing DES for this purpose at the time the plaintiff's mother became pregnant.<sup>564</sup> The plaintiff brought suit, alleging that the defendant had failed to make a reasonable effort to discover whether there were any risks associated with using its product to prevent miscarriages.<sup>565</sup> When the jury found in favor of the plaintiff, the defendant appealed.<sup>566</sup>

On appeal, the defendant argued that it could not be held liable for the plaintiff's injuries because it had not recommended or marketed Diastyl for the prevention of miscarriages.<sup>567</sup> In response, however, the court declared that "[t]he maker of an article for sale or use by others must use reasonable care and skill in designing it . . . so that it is reasonably safe for the purposes for which it intended, and for other uses which are foreseeably probable . . ."<sup>568</sup> The court distinguished between the duty to warn and the duty to test: The defendant was not negligent in failing to inform the

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<sup>560</sup> See *Medics Pharm. Corp. v. Newman*, 378 S.E.2d 487 (Ga. Ct. App. 1989).

<sup>561</sup> *Id.* at 488. DES is a synthetic estrogen that was originally developed to alleviate menstrual symptoms but was later widely marketed for treating women who were at risk for miscarriage. Centers for Disease Control and Prevention, About DES, [http://www.cdc.gov/des/consumers/about/effects\\_daughters.html](http://www.cdc.gov/des/consumers/about/effects_daughters.html). Unfortunately, many female children of the women who had taken DES while pregnant developed clear cell adenocarcinoma, a form of cancer, when they reached puberty. *Id.*; see also Ausness, *supra* note 418, at 386-87.

<sup>562</sup> *Newman*, 378 S.E.2d at 488.

<sup>563</sup> *Id.*

<sup>564</sup> *Id.*

<sup>565</sup> *Id.* at 488-89.

<sup>566</sup> *Id.* at 488.

<sup>567</sup> *Id.*

<sup>568</sup> *Id.* (emphasis in original) (quoting *Ford Motor Co. v. Stubblefield*, 319 S.E.2d 470 (Ga. Ct. App. 1984)).

medical profession of the risk of cancer associated with Diastyl because the risk had not been known at the time the plaintiff's mother ingested the drug.<sup>569</sup> However, drug manufacturers are required to use "reasonable care to provide a product which is reasonably safe for those purposes for which it could foreseeably be used."<sup>570</sup> In this case, the defendant's duty of reasonable care required it to try to discover whether there were any dangers to the unborn fetus in using Diastyl for the prevention of miscarriages.<sup>571</sup>

Although the general principle espoused in *Newman* may be correct, the court's application of the principle to the particular facts of that case is problematic for three reasons. First, the defendant was a distributor, not a drug manufacturer. Therefore, it would be highly unreasonable to expect the company to conduct clinical research on a generic drug like DES. Second, unlike most of the cases discussed in this Article, the defendant in *Newman* did not promote off-label uses of Diastyl. Apparently, the court was willing to impose a duty to test for risks associated with off-label uses simply because the defendant profited from the distribution of its product to physicians who intended to prescribe it for off-label uses. Finally, even if the defendant had engaged in drug testing, it is doubtful that it could have discovered a correlation between ingestion of the drug by pregnant women and subsequent cancer in their unborn daughters. According to the court, the plaintiff's mother took Diastyl in 1963 or 1964, but the cancer risk was not discovered by researchers until the early 1970s.<sup>572</sup> There is no reason to think that the defendant would have discovered this risk ten years sooner if it had engaged in testing.

Plaintiffs have developed an impressive array of tort liability theories in actions against pharmaceutical companies that encourage off-label uses of their products. Although fraud-on-the-FDA, negligence per se and fraudulent misrepresentation theories have not been very successful, some failure-to-warn claims have succeeded. In addition, at least one court has held a drug company liable for failing to test for off-label related risks.

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<sup>569</sup> *Id.* at 489.

<sup>570</sup> *Id.*

<sup>571</sup> *Id.*

<sup>572</sup> *Id.* at 488.

## V. REGULATING THE PROMOTION OF OFF-LABEL USES

A. *Sources of Danger*

Bad things can happen to drug companies that promote and market their products for off-label uses. There are a number of sources of danger, as outlined above. The first source is the FDCA itself. The promotion of off-label uses in violation of the FDCA can constitute misbranding and lead to civil and criminal liability.<sup>573</sup> As the manufacturer of OxyContin discovered, the fines and civil penalties can amount to millions of dollars.<sup>574</sup>

RICO and FCA violations pose a second potential source of risk to pharmaceutical companies that promote and market their products for off-label uses.<sup>575</sup> Cases brought under these statutes usually involve fraudulent schemes to evade restrictions on compensation of off-label uses by Medicaid or other government-sponsored health care programs. Although the drug companies managed to avoid liability in *Hamm* and *Neurontin*, the two RICO cases discussed earlier, RICO remains a potential source of liability.<sup>576</sup> For example, a group of health insurance plans have brought a class action suit against Pfizer, claiming that it engaged in a fraudulent scheme to market Lipitor for off-label uses, which caused them to pay billions of dollars for Lipitor prescriptions that violated federal guidelines for treating cholesterol.<sup>577</sup> In addition to charging Pfizer with fraud and violation of state consumer protection laws, the plaintiffs asserted claims under RICO.<sup>578</sup> Finally, drug companies have been sued in *qui tam* actions brought under the FCA.<sup>579</sup> The defendants prevailed in two of these reported cases—*United States ex rel. Hess v. Sanofi-Synthelabo, Inc.*<sup>580</sup> and *United States ex rel. Rost v. Pfizer*

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<sup>573</sup> Greene, *supra* note 5, at 46.

<sup>574</sup> See *supra* Part II.C.

<sup>575</sup> See *supra* Part III.

<sup>576</sup> See *supra* Part III.A (discussing *Hamm v. Rhone-Poulenc Rorer Pharm., Inc.*, 187 F.3d 941 (8th Cir. 1999); *In re Neurontin Mktg., Sales Practices, and Prods. Liab. Litig.*, 433 F. Supp. 2d 172 (D. Mass. 2006)).

<sup>577</sup> For a discussion of this case, see On Pharma, Off Label Marketing for Lipitor's Now the Focus of a Class-Action Suit (Mar. 30, 2006), <http://pharmamanufacturing.wordpress.com/2006/03/30/off-label-marketing-for-lipitors-now-the-focus-of-a-class-action-suit/>.

<sup>578</sup> *Id.*

<sup>579</sup> See *supra* text accompanying notes 198-362.

<sup>580</sup> No. 4:05CV570, 2006 WL 1064127 (E.D. Mo. Apr. 21, 2006).

*Inc.*<sup>581</sup>—but the manufacturer of Neurontin paid \$430 million to settle a FCA case,<sup>582</sup> and a number of other FCA cases also resulted in large settlements.<sup>583</sup>

Tort law is the third source of danger to drug manufacturers.<sup>584</sup> Although the Supreme Court concluded that fraud-on-the-FDA claims are impliedly preempted by the FDCA,<sup>585</sup> numerous plaintiffs have tried to avoid the preemption bar by invoking the doctrine of negligence per se instead.<sup>586</sup> So far, however, claims based on statutory violations have not been well received by the courts.<sup>587</sup> Fraudulent misrepresentation claims have not fared well either because plaintiffs have had difficulty proving reliance and causation.<sup>588</sup> Failure-to-warn claims have met with mixed results.<sup>589</sup> Defendants have prevailed in most of the reported cases,<sup>590</sup> but plaintiffs have won a few.<sup>591</sup> Finally, at least one court has imposed liability on a distributor of a prescription drug for failing to test for possible side effects from a commonly prescribed off-label use of the drug.<sup>592</sup>

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<sup>581</sup> 446 F. Supp. 2d 6 (D. Mass. 2006), *vacated and remanded*, 507 F.3d 720 (1st Cir. 2007).

<sup>582</sup> *See United States ex rel. Franklin v. Parke-Davis, Div. of Warner-Lambert Co.*, 147 F. Supp. 2d 39 (D. Mass. 2001); Cinquegrana & Lloyd, *supra* note 259.

<sup>583</sup> The website for the organization Taxpayers Against Fraud maintains a list of recent FCA settlements involving drug companies. Taxpayers Against Fraud, Top 20 False Claims Act Cases, <http://www.taf.org/top20.htm> (last visited Mar. 11, 2008).

<sup>584</sup> *See supra* Part IV.

<sup>585</sup> *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001).

<sup>586</sup> *Talley v. Danek Med., Inc.*, 179 F.3d 154, 157 (4th Cir. 1999); *Menges v. Depuy Motech, Inc.*, 61 F. Supp. 2d 817, 829 (N.D. Ind. 1999); *King v. Danek Med., Inc.*, 37 S.W.3d 429, 430-31 (Tenn. Ct. App. 2000); *see supra* Part IV.A.2.

<sup>587</sup> *See Talley*, 179 F.3d at 157; *Menges*, 61 F. Supp. 2d at 829; *King*, 37 S.W.2d at 430-31; *supra* Part IV.A.

<sup>588</sup> *See Talley*, 179 F.3d at 164; *McCauley v. Purdue Pharma L.P.*, 331 F. Supp. 2d 449, 462 (W.D. Va. 2004); *Sita v. Danek Med., Inc.*, 43 F. Supp. 2d 245, 260 (E.D.N.Y. 1999); *Baker v. Danek Med.*, 35 F. Supp. 2d 875, 878 (N.D. Fla. 1998); *Osburn v. Danek Med., Inc.*, 520 S.E.2d 88, 95 (N.C. Ct. App. 1999); *Harden v. Danek Med., Inc.*, 985 S.W.2d 449, 453 (Tenn. Ct. App. 1998); *supra* Part IV.B.

<sup>589</sup> *See supra* Part IV.C.

<sup>590</sup> *Sita*, 43 F. Supp. 2d at 245, 265; *Rhoto v. Ribando*, 504 So. 2d 1119, 1120 (La. Ct. App. 1987); *Formella v. Ciba-Geigy Corp.*, 300 N.W.2d 356, 359 (Mich. Ct. App. 1980).

<sup>591</sup> *See, e.g., Knowlton v. Deseret Med., Inc.*, 930 F.2d 116, 124 (1st Cir. 1991); *Love v. Wolf*, 38 Cal. Rptr. 183, 199 (Ct. App. 1964); *Proctor v. Davis*, 682 N.E.2d 1203, 1217 (Ill. Ct. App. 1997).

<sup>592</sup> *Medics Pharm. Corp. v. Newman*, 378 S.E.2d 487, 488 (Ga. Ct. App. 1989); *see supra* Part IV.D.

*B. Changing the Current Regulatory Policy*

The current regulatory approach to off-label use of drugs and medical devices is inconsistent and incoherent. On one hand, the FDA tolerates and even approves of the widespread prescription of drugs and medical devices for off-label uses. At the same time, the FDA discourages pharmaceutical companies from disseminating information about off-label uses to health care professionals.<sup>593</sup> In addition, federal health care programs often do not reimburse health care providers for off-label therapies. This creates a serious dilemma for drug companies. They have a strong financial incentive to encourage off-label uses of their products by directing promotional efforts at physicians and other health care professionals. At the same time, drug companies that wish to promote off-label uses of their products are often forced to engage in conduct that exposes them to substantial civil and criminal liability.<sup>594</sup>

The rationale for discouraging off-label uses is that some of these uses may be dangerous or ineffective. Fen-phen is perhaps the most famous example of an off-label prescription drug use that posed significant safety risks.<sup>595</sup> The drug fenfluramine was originally approved by the FDA for short-term use by obese patients. However, common off-label uses included use in connection with another drug, phentermine; use of the drug beyond the approved period; and use of the drug by persons who were overweight but not obese.<sup>596</sup> Unfortunately, long-term use of the fen-phen combination caused heart valve damage to many patients.<sup>597</sup> Other examples of drugs that have caused injuries or were determined to be ineffective after they were prescribed for off-label uses include Letrozole, approved for the treatment of breast cancer but prescribed as a fertility drug, and Actimmune, a drug approved to treat two rare diseases but prescribed to treat idiopathic pulmonary fibrosis.<sup>598</sup> Letrozole caused birth defects, and

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<sup>593</sup> Greene, *supra* note 5, at 48.

<sup>594</sup> *Id.* at 67-68.

<sup>595</sup> Fen-phen is a combination of fenfluramine, a serotonergic agent, and phentermine, an amphetamine-like substance. Wilsker, *supra* note 25, at 825-26. Both of these drugs suppress appetite, though in different ways. *Id.*

<sup>596</sup> Salbu, *supra* note 6, at 203.

<sup>597</sup> Greene, *supra* note 5, at 47.

<sup>598</sup> Margaret Z. Johns, *Informed Consent: Requiring Doctors to Disclose Off-Label Prescriptions and Conflicts of Interest*, 58 HASTINGS L.J. 967, 969 (2007).

Actimmune was eventually found to be ineffective for treating pulmonary fibrosis.

The FDA's ambivalent attitude regarding the promotion of off-label uses by drug companies reflects the fact that the agency is faced with two competing regulatory goals, and there is no obvious way to reconcile or balance them. The competing goals are the speedy introduction of new and innovative treatments for disease and the need to assure the public that prescription drugs and medical devices are effective and reasonably safe. While it is beyond the scope of this Article to formulate a fully developed regulatory policy regarding off-label use, it might be useful to examine a few alternatives to the present policy.

We start with the assumption that a complete ban on the promotion of off-label uses would have an adverse effect on public health because it would inhibit the dissemination of information about innovative medical treatments.<sup>599</sup> As long as the FDA allows physicians to prescribe drugs and medical devices for unapproved uses, it makes no sense for the agency to limit access to information about such uses. Therefore, the FDA should revise its current policy to permit drug companies to promote off-label uses of their products in the same manner as they promote approved uses. In order to reduce the risks of off-label use, the FDA should monitor promotional material for accuracy and should require researchers who publish their findings in scientific journals or speak at medical educational programs to disclose any financial interest they may have in the product.<sup>600</sup> At the same time, the FDA should be able to require a drug company to warn doctors when it becomes aware of a risk associated with an off-label use,<sup>601</sup> and if the risk is significant, the agency should have the power to require the manufacturer to prepare a supplemental NDA if it wishes to continue promoting a particular off-label use. To be sure, if drug manufacturers are allowed to freely promote off-label uses of their products, they will have less incentive to undertake the time-consuming and expensive process of seeking FDA approval. However, as we have seen, as long as Medicare and

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<sup>599</sup> Merrill, *supra* note 21, at 1855.

<sup>600</sup> Polubinski, *supra* note 30, at 1033-34.

<sup>601</sup> The FDA currently maintains a website called Drug Watch which provides doctors with information about off-label prescriptions. Johns, *supra* note 598, at 1006; *see also* Stoffelmayr, *supra* note 31, at 276 (arguing for a tort-based duty on the part of drug manufacturers to warn of all demonstrated risks of off-label uses of their products).

Medicaid programs do not reimburse health care providers for off-label uses, drug manufacturers will still have some incentive to seek FDA approval for uses that are currently off-label.

## VI. CONCLUSION

Off-label uses of prescription drugs and medical devices are common and widely accepted within the medical profession.<sup>602</sup> Unfortunately, the FDA restricts the ability of drug manufacturers to promote off-label uses of their products. In addition, government health insurance programs often do not reimburse health care providers for off-label uses of pharmaceutical products. Drug companies who act improperly risk liability for violating the FDCA, RICO, or the FCA. Drug manufacturers may also be subject to tort liability based on theories of negligence per se, fraudulent misrepresentation, failure to warn, and failure to test for risks associated with off-label uses. All of this not only subjects drug companies to substantial financial risks, but also discourages them from providing physicians with useful information about new and effective treatments.

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<sup>602</sup> Merrill, *supra* note 21, at 1854.