

OFF-LABEL MARKETING AS A PREDICATE FOR FALSE CLAIMS ACT LIABILITY

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Liability under the False Claims Act (“FCA”), 31 U.S.C. § 3729-33, can arise when pharmaceutical manufacturers market their drugs for uses that are not specifically approved by the U.S. Food and Drug Administration (“FDA”). Once a new drug is approved under the Food, Drug, and Cosmetics Act (“FDCA”), 21 U.S.C. §§ 301-97, the FDA does not preclude doctors from exercising their professional judgment by prescribing it for indications other than those approved by the FDA, commonly referred to as “off-label” uses. Manufacturers, however, are prohibited from marketing or promoting a drug for off-label uses. 21 U.S.C. §§ 331(d), 355(a) and (d). Even if the information is truthful and the drug’s use beneficial to the patient, off-label promotion by a manufacturer is generally illegal and may subject the manufacturer to an enforcement action, civil liability, or criminal and civil penalties, including penalties under the FCA and various state false claims acts.

I. CONTOURS OF AN “OFF-LABEL” CASE.

A. The Basics.

When a pharmaceutical manufacturer unlawfully markets its drugs to physicians for off-label use, it presumably does so knowing that some of the prescriptions generated will result in claims for reimbursement being submitted to a governmental entity, such as Medicare or Medicaid. For example, as explained below, Medicaid does not normally reimburse off-label prescriptions. Medicaid’s exclusion, combined with the prohibition against manufacturers promoting off-label uses, generated the seminal case of *U.S. ex rel. Franklin v. Parke-Davis*, which recognized that a claim pursuant to the FCA may be predicated on a manufacturer’s illegal off-label marketing of a drug that resulted in submissions of false claims for payment to Medicaid. 147 F. Supp. 2d 39, 52–53 (D. Mass. 2001).

Medicaid’s exclusion of off-label prescriptions is contained in Medicaid’s definition of “covered outpatient drugs.” First, it broadly defines “covered outpatient drugs” as any drug with an FDA approval, 42 U.S.C. § 1396r-8(k)(2)(A) (i), but then limits the definition to exclude drugs “used for a medical indication which is not a medically accepted indication.” 42 U.S.C. § 1396r-8(k)(3). In turn, the statute defines a “medically accepted indication” as an indication that

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is either FDA approved or is included in any of the compendia described in 42 U.S.C. § 1396r-8(g)(1)(B)(i). 42 U.S.C. § 1396r-8(k)(6). At least one court has interpreted the “supported by citations in the compendia” language to hold that states cannot overlay additional requirements, such as the existence of a favorable double-blind clinical study, because “Congress has already stamped its imprimatur on these compendia” and, thus, “applying a more stringent test . . . is effectively denying coverage for those drugs [the state] is legally required to cover.” *Edmonds, et al. v. Levine*, 417 F. Supp. 2d 1323, 1339, 1341 (S.D. Fla. 2006).

Accordingly, a typical off-label FCA case alleges that the manufacturer violated the FDA rule against promoting a drug for an off-label use, which induced physicians to prescribe the drug for an off-label purpose that they otherwise would not have, and that certain of those prescriptions were submitted to a governmental entity, such as Medicaid, for reimbursement. For instance, Eli Lilly & Company recently settled a FCA case involving the off-label marketing of Zyprexa for \$1.42 billion. The United States¹ alleged that Eli Lilly caused claims for payment for off-label prescriptions of Zyprexa to be submitted to the Medicaid Program, the TRICARE program, and the Federal Employees Health Benefits Program, and caused purchases to be made by the Departments of Defense, Labor, and Veterans Affairs, the Bureau of Prisons, and “Public Health Service Entities.” See Settlement Agreement at 3, *U.S. ex rel. Rudolph, et al. v. Eli Lilly & Co.*, Civ. Action No. 03-0943 (E.D. Pa. Jan. 15, 2009). The United States contended that

Eli Lilly knowingly promoted the sale and use of Zyprexa to . . . health care professionals . . . for certain uses for which the [FDA] had not approved . . . and these unapproved uses were not medically accepted indications for which the United States and State Medicaid programs provided coverage. . . . As a result of the foregoing alleged conduct . . . contends that Eli Lilly knowingly caused false and/or fraudulent claims to be submitted to the United States . . . for these unapproved uses.

Id. at 4.

Such a case presumes, and the defendant cannot dispute, that the government would not have paid for the off-label prescription if it had known that the physician’s prescribing decision was improperly influenced by the manufacturer’s illegal conduct. *Parke-Davis*, 147 F. Supp. 2d at 53. While most off-label FCA cases are based on this basic premise, in practice the cases are far more complicated and, as discussed below, often include allegations that the manufacturer paid illegal kickbacks as part of its off-label marketing efforts.²

1. The United States intervened in *U.S. ex rel. Rudolph, et al. v. Eli Lilly & Co.*, which was the consolidation of four actions filed by relators.

2. Despite a relator’s choice of forum, a FCA case may be transferred to a multidistrict litigation (“MDL”) for consolidated pre-trial discovery. See, e.g., *California ex rel. Vicente v. Eli Lilly and Co.*, No. C 07-04911 (N.D. Cal.) (involving the off-label marketing of Zyprexa). But see *U.S. ex rel. West v. Ortho-McNeil Pharmaceutical*, No. 03 C 8239, 2007 WL 2091185 (N.D. Ill. July 20, 2007) (involving FCA allegations regarding Levaquin and Ultram,

B. Off-Label Marketing Schemes and Safe Harbors.

The method through which manufacturers deliver unlawful off-label promotional messages is fairly consistent across offending manufacturers, although the particular design and implementation may vary. The media of delivery includes printed materials, journal articles, “detailing” visits to physicians by sales reps, and lectures in various settings—from luncheons to destination seminars—delivered to prescribers by influential peers. The content of the materials is nearly always carefully crafted by the manufacturer to convey the off-label message without attracting regulatory scrutiny, often using colloquialisms and other subtleties, such as referring to “expanded” or “emerging” uses, which are, in reality, euphemisms for off-label uses. The mode of delivery is itself often carefully chosen to provide a veneer of unbiased legitimacy and conceal the manufacturer’s role in crafting the message and funding its delivery.

For a number of years, a “safe harbor” existed for manufacturers that complied with the FDA Modernization Act of 1997 (“FDAMA”), 21 U.S.C. § 360aaa. The FDAMA set forth limited ways in which manufacturers could provide journal articles and publications to physicians about unapproved uses of approved products. The safe harbor provided that, as long as a manufacturer complied with the FDAMA, the FDA would not use its dissemination of such materials as evidence of the manufacturer’s intent that the product be distributed for an off-label use. In *U.S. ex rel. Franklin v. Parke-Davis*, No. Civ. A. 96-11651-PBS, 2003 WL 22048255, at *2 (D. Mass. Aug. 22, 2003), the court explained that even truthful off-label marketing that is ineligible for federal safe harbor protection would support a claim for causing false claims to be presented under 31 U.S.C. § 3729(a)(1).

On September 30, 2006, the FDAMA was allowed to sunset and, on January 13, 2009, the FDA issued new guidance on manufacturers’ dissemination of publications on unapproved uses of approved drugs to healthcare professionals and entities. See *Guidance for Industry on 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*, at *2, available at, <http://www.fda.gov/oc/op/goodreprint.html>. While the guidance provides no legally binding assurance of a safe harbor, it states:

if a manufacturer follows the recommendations described in Section IV of this guidance, FDA does not intend to consider the distribution of such medical and scientific information in

and noting the off-label marketing claims were remanded from the MDL court). These cases are sometimes transferred because allegations that a manufacturer made false or misleading statements about the safety and efficacy of a drug are frequently at issue in personal injury, products liability, and securities fraud actions, all of which may give rise to MDLs. In fact, while there are no off-label allegations at issue, a FCA action currently being prosecuted by this author against Bayer for claims involving Baycol has recently been transferred to a products liability MDL. See *U.S. ex rel. Simpson v. Bayer*, Civil Action No. 08-cv-5758 (D. Minn.) (transferee court); Civil Action No. 06-cv-4796 (D.N.J.) (transferor court).

accordance with the recommendations in this guidance as establishing intent that the product be used for an unapproved new use. However, if a manufacturer engages in other conduct that unlawfully promotes an unapproved use of a medical product . . . such other conduct may result in enforcement action.

Id. at *5–6. It is clear from the guidance’s stated purpose that the FDA finds value in the distribution of credible medical information that is distributed in accordance with its guidance. *Id.* at *2. Yet, the FDA reminds the industry that any deviation from the guidance, even if the underlying information is truthful, may result in a civil or criminal action.

C. The Problematic Nature of a FCA Case Based on Third-Party Reimbursements.

Manufacturers’ false statements regarding a drug’s safety and efficacy, which are designed to induce physicians to prescribe a drug for an off-label purpose, can support claims under 31 U.S.C. § 3729(a)(2) for making false statements in order to get a false claim paid or approved. However, claims brought under 31 U.S.C. § 3729(a)(2) now require an assessment of the potential application of *Allison Engine Co. v. U.S. ex rel. Sanders*, ___ U.S. ___, 128 S. Ct. 2123 (2008). *Allison Engine* was a FCA case involving subcontractors’ that submitted invoices, seeking payment for work that was not performed in accordance with specifications, which were submitted to shipbuilders contracted by the United States Navy. *Id.* at 2126-27. In holding that the subcontractors’ invoices, which falsely certified that they complied with Navy specifications, did not constitute false claims to the government, the U.S. Supreme Court grafted a new intent requirement into subsection (a)(2), at least in some circumstances, stating that “a subcontractor violates § 3729(a)(2) if the subcontractor submits a false statement to the prime contractor intending for the statement to be used by the prime contractor to get the Government to pay its claim.” *Id.* at 2130. Thus, (a)(2) requires proof “that the defendant made a false record or statement for the purpose of getting a false or fraudulent claim paid or approved by the Government.” *Id.* The defense bar argues that this holding applies beyond subcontractors and applies to all § 3729(a)(2) claims involving entities that do not directly submit claims to the Government. Hence, any time such a claim is asserted against a drug manufacturer that did not sell products directly to the government (*i.e.*, where prescriptions are reimbursed through a governmental entity such as Medicare or Medicaid), such a defense is likely to be raised.

But, a drug manufacturer’s misconduct is different in nature than a false certification of compliance with specifications that gives rise to a § 3729(a)(2) claim against a subcontractor. The drug manufacturer is not in a subcontractor role of filling an advance order for specific goods, but rather an independent actor in the stream of prescription drug commerce whose intentional miscon-

duct taints the reimbursement claims submitted by downstream actors such as physicians and pharmacists. See *Parke-Davis*, 2003 WL 22048255, at *5; *U.S. ex rel. Marcus v. Hess*, 317 U.S. 537, 543 (1943) (as to potential FCA liability of upstream actor in bid-rigging scheme, the court found a claim was stated because the “fraud did not spend itself with the execution of the contract. . . . Its taint entered into every swollen estimate which was the basic cause for payment of every dollar paid by the P.W.A. . . .”); *Parke-Davis*, 147 F. Supp. 2d at 52 (FCA claim properly stated against drug manufacturer predicated on off-label promotion); *In re Pharmaceutical Average Wholesale Price Litigation*, 491 F. Supp. 2d 12, 16 (D. Mass. 2007) (FCA claim properly stated by allegations that drug manufacturer manipulated average wholesale price upon which government calculated drug reimbursement).

The physician’s freedom to write prescriptions for off-label indications raises the question: how can there be liability against the manufacturer when there is an intervening free agent? The answer is that the government has successfully wielded a presumption that the manufacturer’s illegal promotion of the off-label use unduly influenced the physicians to write a greater number of off-label prescriptions than they otherwise would have. In the seminal case of *U.S. ex rel. Franklin v. Parke-Davis*, the court denied the defendant’s motion for summary judgment on those grounds, holding that “the participation of doctors and pharmacists in the submission of false Medicaid claims was not only foreseeable, it was an intended consequence of the alleged scheme of fraud.” 2003 WL 22048255, at *5 (quoting *Parke-Davis*, 147 F. Supp. 2d at 52–53).

Such a presumption is justified because the offending manufacturers typically promote off-label uses through various methods disguised as educational in nature and purport to impart unbiased scientific fact, when, in reality, they are carefully crafted marketing campaigns. Indeed, drug company marketing departments often analyze the success of these efforts, for example, by tracking the targeted physicians’ prescribing levels and comparing them to marketing expenditures (including arguable kickbacks such as consulting fees, conventions, and honoraria). This information enables marketers to refine these campaigns to improve their effectiveness at generating off-label prescriptions.

There is also the puzzling question of just how are “false” claims being submitted in the first place, since an accurately completed reimbursement form would reflect off-label usage and would simply be disallowed as non-qualifying. The very fact that the prescriptions are being paid, however, reflects the reality that the claim form does not require sufficient information to identify the off-label nature of prescriptions that were the result of illegal marketing practices. See *Parke-Davis*, 2003 WL 22048255, at *4.

Rather than delving into the details of particular claim submissions, courts have instead focused on the conduct of the manufacturers and presumed that their conduct caused a significant percentage of claims to be “false,” and that a significant percentage of those claims were in fact submitted to the government.

In *U.S. ex rel. Kennedy v. Aventis Pharmaceuticals, Inc.*, 512 F. Supp. 2d 1158, 1167 (N.D. Ill. 2007), the court denied a Rule 9(b) motion to dismiss, finding that “specific facts . . . regarding particular claims were and are not likely within relators’ reach” and, moreover, that “[g]iven the significant proportion of medical care in this country that is financed by Medicare and Medicaid, relators have drawn a reasonable inference that claims for reimbursement regarding off-label uses of Lovenox were submitted to the federal government or the State of Illinois for payment.” Likewise, in *U.S. ex rel. Rost v. Pfizer, Inc.*, 507 F.3d 720, 732 (1st Cir. 2007), the relator alleged that a significant percentage of Genotropin prescriptions were for off-label uses. The First Circuit stated that it was “not irrational to infer that, given the large percentage of children and the elderly who are insured under federal health programs, some false claims for Genotropin reimbursement were submitted to the government.” *Id.* However, the strength of that inference was undercut by the criminal information that acknowledged “[i]n most, if not all, instances, patients taking Genotropin [for off-label uses] paid . . . out-of-pocket without reimbursement from any public or private third-party payors.” *Id.* Consequently, without any government reimbursement, the First Circuit concluded the complaint did not adequately particularize that false claims were submitted to the government. *Id.*

D. Additional Allegations that Arise in Off-Label Cases.

1. Kickback Claims.

Manufacturers engaging in illegal off-label marketing often use incentives, in various forms, to induce physicians to attend educational presentations, participate in consulting arrangements, and review clinical materials, all of which are basically thinly veiled off-label promotions. Such incentives can constitute kickbacks and form an independent basis for liability under the FCA; however, such claims bring with them another layer of thorny issues.

For example, in *Parke-Davis* the court dismissed kickback claims that accompanied off-label allegations on the basis that the relator failed to allege the requisite false certification of compliance with the anti-kickback statute. 147 F. Supp. 2d at 53–54. Simply violating the federal anti-kickback statute is not itself “a *per se* violation of the FCA. In order for the anti-kickback violation to be transformed into an actionable FCA claim, the government must have conditioned payment of a claim upon the claimant’s certification of compliance with the anti-kickback provision.” *Id.* at 54.

In *U.S. ex rel. Franklin v. Pfizer, Inc.* the court denied a motion to add FCA claims predicated on kickbacks because of undue delay and prejudice, and because the allegation that a manufacturer paid “kickbacks to physicians who wrote prescriptions to patients who submitted the prescriptions to pharmacists who submitted reimbursement claims to state and federal Medicaid agencies”

was too “attenuated” a chain of causation to establish a claim under the FCA. No. Civ. A. 96-11651-PBS, 2002 WL 32128635, at *1 (D. Mass. Feb. 6, 2002). The court did recognize that a viable claim might arise when the “kickbacks were coupled with express certifications.” *Id.*

2. Misbranding Claims.

Manufacturers engaged in illegal off-label marketing may also be found to have violated regulations against “misbranding.” FDA regulations prohibit “labeling” (a term broadly defined to cover many forms of manufacturer communications) that provides inadequate directions for use, contains false or misleading information, or includes information about unapproved uses. 21 U.S.C. §§ 331(a), 352(a) and (f); 21 C.F.R. § 202.1; see also *Parke-Davis*, 147 F. Supp. 2d at 44. Drugs with such labeling are considered “misbranded,” and the sale of misbranded drugs is expressly prohibited. 21 U.S.C. § 333. Allegations of misbranding are typically based on two grounds: (1) that a product promoted for off-label use is misbranded because its directions are inadequate for the unapproved intended use, 21 U.S.C. 352(f); and/or (2) that the manufacturer disseminated “false and misleading” information regarding the product, 21 U.S.C. 352(a). See George S. Craft, Jr., *Promoting Off-Label in Pursuit of Profit: An Examination of a Fraudulent Business Model*, 8 Hous. J. Health L. & Pol’y 103, 108 (2007) (citing Sentencing Memorandum of the United States, *U.S. ex rel. Warner-Lambert Co. LLC*, Crim. No. 04-10150 RGS, at 4–5 (D. Mass., filed June 2, 2004)); see also U.S.D.O.J. Press Release concerning settlement with Jazz Pharmaceuticals, Inc. and Orphan Medical, Inc., available at, <http://www.usdoj.gov/usao/nye/pr/2007/2007jul13a.html> (describing the defendant’s guilty plea for felony misbranding, which was based upon its off-label promotions).

II. RECENT OFF-LABEL SETTLEMENTS.

Recent civil recoveries and criminal fines and restitution in off-label cases have been quite substantial. Settlements have ranged from \$9.8 million against Medicis Pharmaceutical Corp. for off-label promotion of Loprox to a record \$1.42 billion against Eli Lilly for illegally marketing Zyprexa for off-label use. In addition, significant criminal fines suggest that the government takes a strong interest in these cases and views them as serious violations of the law.

