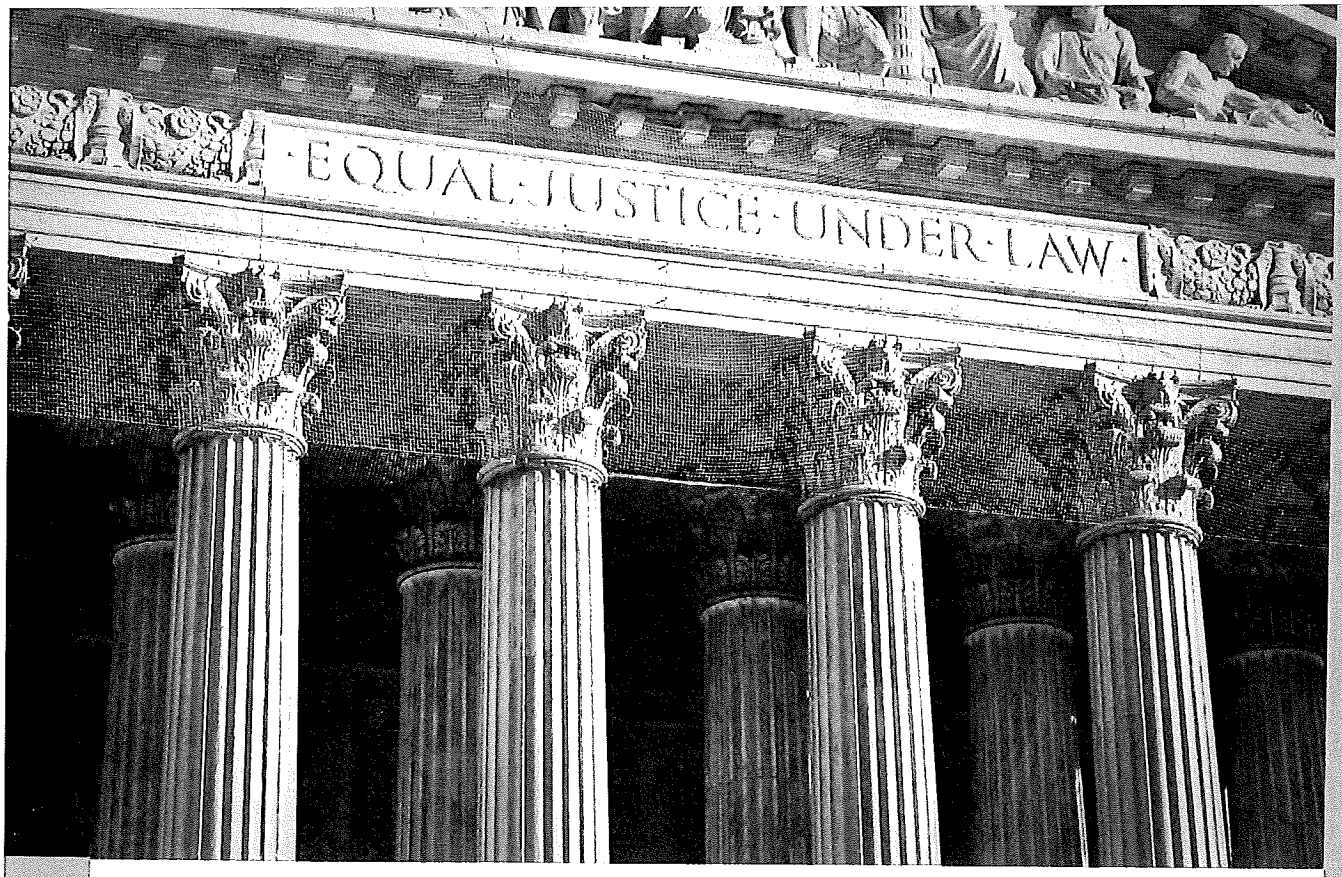
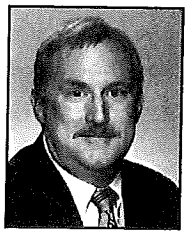


Developments in Enforcement of Off Label Promotional Activities

By Mark Carlisle Levy and Emily R. Schulman

Since 2009, when the second edition of Off-Label Communications: A Guide to Sales & Marketing Compliance was released, there have been many interesting and challenging developments facing drug and device manufacturers arising from off-label use of approved products. First, the regulation of off-label promotional activity has remained a high priority for the government. Government enforcement efforts have been on the rise, with an increased number of criminal and civil prosecutions, record-breaking settlements, calls for increased focus on individual culpability, a renewed debate about the merits of prosecuting high-level executives under the Park doctrine, and increasing use of administrative sanctions to hold individuals accountable for health care fraud violations. At the same time, there is growing controversy about the constitutional implications of prosecuting truthful off-label promotion and renewed efforts – through the appellate process, declaratory judgments, and FDA rulemaking – to clarify and circumscribe the contours of proscribed off-label activity. In sum, changes in the climate surrounding off-label sales and marketing necessitate corporate vigilance to best prepare for the challenges which these changes pose.



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Settlement Trends: Size and Sales and Marketing Practices

The past three years have been marked by landmark health care fraud settlements. No sooner had the United States Attorneys' Office for the Eastern District of Pennsylvania broken the $1 billion threshold in 2009, settling off-label promotion claims with Eli Lilly over the company's marketing of Zyprexa, than the District of Massachusetts announced a $2.3 billion settlement later that same year with Pfizer over the company's misbranding of Bextra, among other products. Recently, in another record-setting settlement, GlaxoSmithKline agreed to pay $3 billion to settle civil and criminal charges pertaining to its misbranding of Avandia as well as claims relating to two other prescription drugs. Continuing this billion-dollar settlement trend, Abbott Laboratories reached an agreement with the United States Attorneys' Office for the Western District of Virginia in 2012 to settle adulteration and misbranding claims pertaining to Depakote for $1.5 billion. Each of these billion-dollar settlements has featured a "blockbuster" product whose marketing entailed off-label promotional claims, generated billions of dollars in sales, spanned from four to five years, and was actively marketed to physicians for off-label use. In some cases, the off-label use posed a potentially serious safety risk to arguably vulnerable victims. A telling sign of how quickly and how far the settlement bar has been raised is that the government's $950 million settlement with Merck in 2011 over the company's off-label promotion of Vioxx, its $600 million settlement with Allergan in September 2010 for promotional activities associated with Botox , and its $423 million settlement with Novartis in that same month resolving off-label marketing claims pertaining to Trileptal.

Of note, the past three years have also seen a notable expansion in government enforcement activity against medical device manufacturers, punctuated by high-profile prosecutions against Synthes, Inc. in 2011 and Stryker Biotech, Corp. in 2012. Further, settlements with Endoscopic Technologies, Atricure and Novo Nordisk over off-label promotion have ranged from $1 million to $25 million.

Prosecution of Individuals: Increasing Focus on Individual Culpability, Park Doctrine, Administrative Sanctions

Individual Culpability

Since 2009, government health care fraud enforcement efforts have focused increasingly on individual culpability in conjunction with corporate liability, but the government encountered some high profile setbacks as well as successes in its individual prosecutions. Among the more noteworthy individual prosecutions during this period, was that of Scott Harkonen, former InterMune Chief Executive Officer and Board member, who was convicted of wire fraud based on the company's issuance of a press release announcing positive results from a failed clinical trial of Actimmune for the treatment of a particular type of lung disease. Even though Actimmune was not indicated for the treatment of that lung condition, off-label prescriptions for that condition accounted for a very large percentage of the product's sales. InterMune itself entered into a deferred prosecution agreement with the government for its marketing and promotion practices relating to Actimmune.

The prosecution of former GlaxoSmithKline Vice President and Associate General Counsel, Lauren Stevens, was among the most controversial healthcare fraud-related individual prosecutions during this period. Ms. Stevens was criminally prosecuted for obstruction of justice and related charges based on her allegedly false and/or misleading statements to the government when responding to an FDA request for information. Some members of the legal community viewed Ms. Stevens' prosecution as an assault on or at least threat to fundamental principles of legal advocacy. Indeed, Ms. Stevens' allegedly false statements to FDA were made in the context of responding as company counsel to an FDA inquiry. Many believed that her statements were well within the bounds of legitimate legal advocacy. Moreover, it was undisputed that, before Ms. Stevens made any of her contested representations to the government, sophisticated outside counsel with years of specialized experience in FDA law vetted them, thereby potentially vitiating the requisite mens rea for criminal obstruction and potentially insulating her criminal wrongdoing based on the advice of counsel. The trial judge overseeing the Stevens prosecution dismissed the case not once, but twice. It was the first Rule 29 motion the district court judge had ever granted in his eight years on the federal bench. In doing so, he underscored the "enormous potential for abuse in allowing the prosecution of an attorney for the giving of legal advice," found that Ms. Stevens "should never have been prosecuted,"

and concluded that "only with a jaundiced eye and with an inference of guilt that's inconsistent with the presumption of innocence could a reasonable jury ever convict" her.

While the Stevens prosecution ultimately foundered due to its aggressive interpretation of legal doctrine, the government suffered other high-profile defeats in its prosecution of individuals since 2009 due to fundamental shortcomings in its factual investigations and disclosures. The prosecution of Stryker Biotech Corp.'s Chief Executive Officer and three of its former high-level sales managers in January 2012 on felony misbranding and related criminal charges pertaining to the marketing of an unapproved device to generate human bone growth marked one such defeat. Just days into the anticipated six-week trial, the government dismissed all charges against the individual defendants outright and dismissed all 13 felony counts against the company, settling for one misdemeanor misbranding count against the company. The government's theory of the case had been that Stryker defrauded the surgeons who used the company's device off-label to promote human bone growth, but the government neglected during its multi-year investigation to confirm its theory with the so-called victims, and the surgeon's themselves denied that Stryker's sales representatives defrauded, misled or influenced the medical decisions at issue.

Park Doctrine

The revival of the *Park* doctrine in 2007 through the prosecution of three top executives from Purdue Pharmaceuticals in 2007 on misdemeanor misbranding charges dovetailed with the government's increased commitment to holding individuals accountable for corporate health care fraud violations. At the same time, it sparked much debate and discussion about the pragmatic merits and doctrinal legitimacy of strict liability criminal prosecutions.

While the government has exercised restraint in its use of the *Park* doctrine to prosecute individuals for health care fraud violations, it has nonetheless resorted to the Responsible Corporate Officer doctrine more than once in recent years. In 2009, the government charged Synthes, Inc., its wholly owned subsidiary Norian Corp., and four high-level Synthes executives with criminal charges stemming from the allegedly unauthorized clinical trials the company conducted of its Norian-branded cements. According to the government, the company promoted the use of these cements, which are deemed medical devices and are approved for use elsewhere in the body, in the spinal surgeries of 200 patients with fractured vertebrae, even though an FDA-approved label warned against such use, and pilot studies allegedly showed that they posed grave safety risks to spinal patients.

In 2009, four Synthes executives pled guilty under the *Park* doctrine to one count of misdemeanor misbranding – the only charge the government had brought against them. Nonetheless, at their sentencing hearing in 2011, the government took an aggressive stance – introducing, over the defendants' objections, evidence of the defendants' "false," "fraudulent," "deceptive," and "intentionally deceiving" conduct. This evidence convinced the judge that there was an "unparalleled" "pattern of deception," which in turn contributed to his sentencing each of the defendants to a term of imprisonment at the higher end of the federal sentencing guidelines.

Also, in 2011, Mark Hermelin, former CEO and Chairman of K-V Pharmaceuticals' Board of Directors, pled guilty to an Information charging him under the *Park* doctrine with two counts of misdemeanor misbranding based on the company's distribution of oversized morphine tablets. Harmelin was sentenced to 30 days' imprisonment. The previous year, the Office of Inspector General made a formal determination to exclude him from participation in federal health care programs based on activities unrelated to this conviction for twenty years.

Debarment and/or Exclusion: An Ever-Present and Growing Risk

The government has been increasingly aggressive in recent years in using administrative remedies to sanction individuals for health care fraud violations. Since 2009, there has been a steady rise in the volume and pace of FDA debarment and OIG exclusion proceedings. Even those individuals prosecuted under the *Park* doctrine have been subject to these sanctions. In March 2008, the Office of the Inspector General for the Department of Health and Human Services imposed a 12-year bar on the three Purdue executives who plead guilty to misdemeanor misbranding under the *Park* doctrine, even though the parties agreed that none of the excluded individuals had personal knowledge of the misbranding conduct. On appeal, in August 2012, the Court of Appeals for the District of Columbia Circuit held that, for purposes of the debarment statute, a "misdemeanor relating to fraud" requires only that the criminal conduct at issue have a factual "connection with" fraud, and not that the misdemeanor offense itself share all the "core elements" of fraud. This case of first impression signals

that executives who plead guilty under the *Park* doctrine still face grave risk that severe administrative sanctions could follow from conduct for which they lacked any criminal intent.

Legal Challenges: First Amendment Issues, Scope of FDCA

The legal principles underlying the criminal prosecution of off-label promotion have been subject to continued challenge since 2008. The Supreme Court's decision in *Sorrel v. IMS* reinvigorated the First Amendment challenges to criminal prosecution of off-label promotional activities. While the case itself was not about off-label promotion, it threw into question whether content- and speaker-based regulations on speech are subject to conventional intermediate scrutiny or an even heightened level of scrutiny. Moreover, as Justice Breyer warned in his dissent, the case arguably lays the conceptual foundation for dismantling the FDA's regulatory regime, particularly as applied to off-label promotion. In the wake of the Supreme Court's decision in *Sorrell*, the Second Circuit invited supplemental briefing in *Caronia*, a pending criminal appeal of a pharmaceutical sales representative who was convicted of misbranding, based in part on his allegedly truthful off-label promotional activities. Eleven major drug and device manufacturers submitted an amicus brief in support of Caronia's First Amendment challenge.

In 2011, Par Pharmaceuticals launched its own challenge to FDA's regulation of off-label promotional speech when it filed a declaratory judgment complaint to determine whether truthful, on-label promotional speech could expose a company or its employees to criminal misbranding charges if it occurred in a setting ripe for off-label use of the product at issue.

Perhaps in response to renewed First Amendment debates, FDA solicited public comments in 2011 regarding the proper scope of "scientific exchange" and the dividing line between scientific exchange and promotional activity.

New FDA Guidance: Social Media, Scientific Exchange v. Promotional Activity

FDA's express recognition of social media as an additional dimension and domain of potential off-label activity marks another key development in the legal landscape of health care fraud since 2009. In 2011, FDA issued Draft Guidance on Responding to Unsolicited Requests for Off-Label Information in Public Forums to address, in part, the complications that can arise from unsolicited requests for medical information posted on social media. The FDA guidance counsels manufacturers to respond privately, in one-on-one communications, when responding to such requests. The Guidance further provides that FDA does not intend to use responses that comply with its guidance as evidence of the manufacturer's intent that its product be used for unapproved uses. The Guidance has provided further grist for argument over the scope of the governments regulation of speech and opened the door for many issues relating to what is or is not permissible when communicating about any off-label use, even when such use is permissible by the healthcare professional to prescribe.

The developments in off-label use and promotion of pharmaceutical products over the past three years warrants attention. Hopefully, the Third Edition of *Off-Label Communications* will assist lawyers and non-lawyers in understanding why.