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DOJ Teaches a Lesson in Healthcare Marketing

Recent DOJ off-label cases provide important lessons on risk mitigation in marketing and promotional practices. Study up and you just might protect your company when it matters most.

By Robert Brady, Meredith Manning, Peter Spivack, Stefanie Solomon and Allison Stanton

In a major enforcement strategy shift, the U.S. Department of Justice (DOJ) has taken firm control of enforcement against pharmaceutical and biotech manufacturers. Both "Main Justice" in Washington and various U.S. Attorney Offices around the country now enforce against pharmaceutical companies through not only the Food, Drug, and Cosmetic Act, but also the Anti-Kickback statute and the False Claims Act. Within a span of just two months, the DOJ signaled — via recent settlements — how its use of both civil and criminal enforcement tools will change the way companies promote and market therapeutic products in the future. These cases bear important lessons for counsel seeking to mitigate risk and defend against government investigations and will no doubt quickly be incorporated into the discovery and litigation strategy of plaintiffs' counsel in products liability, false claims act, and shareholder derivative actions.

On December 21, 2005, the DOJ announced that Eli Lilly and Company (Lilly) agreed to plead guilty to a single misdemeanor count and pay a total of $36 million to settle criminal charges and civil allegations related to the company's marketing of its drug Evista, which is approved for the treatment of osteoporosis in post-menopausal women. Signaling DOJ control over the settlement, the Consent Decree mirrors the content of Corporate Integrity Agreements generally drafted by and enforced by the HHS Inspector General.

On October 17, the DOJ announced that the Swiss company Serono, S.A., along with its U.S. subsidiaries, will pay $704 million to settle criminal charges and civil allegations related to the company's marketing practices for its AIDS wasting drug, Serostim. This represents the largest settlement to date concerning allegations of illegal "off-label" promotion and is among the largest concerning health care fraud. Serono has agreed to plead guilty to two felony counts of conspiracy: (1) conspiracy to distribute an unapproved and adulterated medical device, and (2) conspiracy to pay illegal remuneration to health care providers to induce referrals to pharmacies for Serostim — payment for which was made by Medicaid.

Both cases demonstrate that the government continues to expand the nature and extent of company conduct it will investigate, and that it will pursue those investigations vigorously. The settlements also reveal some clues regarding when the government decides to seek felony charges versus reduced misdemeanor charges against a company for off-label promotion. Importantly, these cases further highlight the fact that when enforcing the prohibitions of the FDCA against off-label promotion, the DOJ is strongly scrutinizing practices in pharmaceutical and biotech companies that have not traditionally been investigated or evaluated by FDA. These practices include uses of:

- Continuing medical education
- Advisory boards and consultants
- Incentive compensation
- Market research
- Business planning documents, and
- Responses to unsolicited requests for information

These cases are also notable in that both Serono and Lilly were able to preserve their critical ability to sell products covered under federal health insurance programs. This was accomplished in two different ways: in Serono's case, by limiting the criminal plea to one U.S. subsidiary, Serono Laboratories, Inc.; in Lilly's case, by pleading to a misdemeanor under the FDCA. All Serono U.S. subsidiaries, however, will be subject to a

Corporate Integrity Agreement (CIA) with the Department of Health and Human Services Office of Inspector General (the OIG) for the next five years. Lilly entered into a consent decree that imposes similar obligations and also permanently enjoins the company from promoting Evista for unapproved uses.

Enforcement Environment in the United States

The promotional activities of pharmaceutical companies continue to be a major focus of enforcement actions by the DOJ. In 2004, Pfizer Inc, entered into a $430 million settlement with the government to settle charges that it had illegally promoted its anti-epileptic drug, Neurontin, for an array of unapproved uses, including pain and bipolar disorder. The charges arose out of a *qui tam* or whistleblower lawsuit brought under the federal civil False Claims Act (FCA) by a former employee who painted a picture of a "comprehensive scheme" devised by the company to promote Neurontin for off-label uses. The Neurontin case stands for the novel proposition that a company's off-label promotion is a violation of the False Claims Act if the promotion results in submission of an off-label claim for reimbursement to a federal health care program. The Neurotin case may have established a new standard that it need only be "reasonably foreseeable" that a company's conduct will result in a false Medicaid claim.

The Neurontin case also created an enforcement environment where a disgruntled former employee poses a substantial threat to a company. We believe that there are upwards of 200 pending *qui tam* cases involving allegations of off-label promotion by pharmaceutical companies.

Additionally, it is not necessarily the size of the market for a particular product that puts a company at risk of DOJ investigation. For example, Novo Nordisk recorded only $2.6 million in sales of an insulin product for the first nine months of 2005. It recently announced receipt of a subpoena from the U.S. Attorney for the Eastern District of New York requesting documents related to marketing and promotion of the insulin product. Thus, pharmaceutical companies in markets of all sizes need to be wary of the current enforcement environment.

The Serono Case

The Serono case is the largest settlement surrounding drug promotion. It arose from three *qui tam* actions filed by former sales representatives against the company alleging that Serono knowingly caused false or fraudulent claims to be submitted for reimbursement by Medicaid. Specifically, the complaints alleged that Serono sales representatives used a bioelectrical impedance analysis (BIA) test to "measure" patients' body mass wasting, and that sales representatives were further instructed to manipulate the BIA readings to suggest that patients without AIDS wasting be prescribed Serostim. The whistleblowers also alleged that Serono offered prescribers trips to France in exchange for writing a certain number of prescriptions for Serostim within a set period of time.

The Serono Criminal Settlement

Serono Labs pled guilty to two felony counts: (1) conspiracy to distribute an unapproved and adulterated medical device, and (2) for conspiracy to pay illegal remuneration to health care providers to induce referrals to pharmacies for Serostim — payment for which was made by Medicaid. The government's charging document describes the basis for these charges:

Count One: Through use of unapproved diagnostic software (a device under the Federal Food, Drug, and Cosmetic Act), Serono launched a campaign to convince prescribers that "body cell mass" — rather than weight loss, which the company had used as the clinical endpoint in its clinical investigations supporting approval of the drug — was the true measure of AIDS wasting. Around the time of Serostim's approval, protease inhibitors were also approved by the FDA. These drugs dramatically reduced the number of patients suffering from AIDS wasting, and thus, the demand for Serostim. By "redefining AIDS wasting," the company aimed to artificially expand the Serostim market.

Count Two: To further boost lagging sales, the company initiated a "6m-6 Day Plan" through which representatives were instructed to offer financial incentives to thought leaders and other high prescribers to meet a targeted sales increase of $6 million within six days. Physicians were offered an all-expense paid trip to the International Conference on Nutrition and HIV Infection in Cannes, France, in exchange for the increased prescribing of Serostim.

Serono's criminal penalties for these violations total $137 million.

The Serono Civil Settlement

Under the Civil Settlement agreement, Serono will pay more than $560 million to settle liabilities relating to payments made by state Medicaid and federal healthcare programs for Serostim during the time of the illegal conduct. The government agreed to allow Serono-owned companies other than Serono Labs to continue receiving reimbursement under federal healthcare programs. The government also released Serono from civil claims related to the Serostim promotional conduct.

The Serono Corporate Integrity Agreement

The Corporate Integrity Agreement (CIA) signed by all U.S.-Serono affiliates obligates the company to establish a comprehensive compliance program and develop policies and procedures spanning a variety of topics. The Serono CIA is similar to one in place between the OIG and Pfizer as a result of the Neorontin case. Notable differences exist between the two, however. First, there is a substantively heightened focus on the funding and conduct of medical education programs found in the Serono CIA. Second, Serono is obligated to implement policies and procedures relating to compensation to ensure that financial incentives do not encourage sales and marketing personnel to engage in improper promotional, sales, and marketing practices. Finally, the Serono CIA prohibits medical information staff from responding to requests for off-label information unless the request is made in writing.

The Lilly Case

Lilly agreed to plead guilty and to pay $36 million in connection with its illegal promotion of its pharmaceutical drug Evista. In pleading guilty to a misdemeanor count of misbranding Evista, the Indianapolis-based company agreed to pay a $6 million criminal fine and forfeit to the United States an additional sum of $6 million. In addition, Lilly has agreed to settle civil FDCA liabilities by entering into a Consent Decree of Permanent Injunction. As part of the Consent Decree, Lilly agreed to pay $24 million in equitable disgorgement. The criminal and civil cases were filed in the U.S. District Court for the Southern District of Indiana.

The Lilly Criminal Settlement

The information alleges that the first year's sales of Evista in the United States were disappointing compared to Lilly's original forecast. In October of 1998, the company reduced the forecast of Evista's first year's sales in the United States from $401 million to $120 million, and an internal business plan noted a "disappointing year versus original forecast." Thus, according to the government, Lilly sought to broaden the market for Evista by promoting it for unapproved uses.

Lilly's strategic marketing plans and promotion touted Evista as effective in preventing and reducing the risk of diseases for which the drug's labeling lacked adequate directions for use. Lilly's Evista brand team and sales representatives promoted Evista for the prevention and reduction in risk of breast cancer, and the reduction in the risk of cardiovascular disease. Lilly promoted Evista as effective for reducing the risk of breast cancer, even after the FDA rejected Lilly's proposed labeling that Evista reduced "the frequency of newly diagnosed breast cancer" in those taking Evista compared to placebo.

Although not charged in the information, it is notable that a federal court granted AstraZeneca a preliminary injunction against Lilly in 1999 under the Lanham Act to block the firm from promoting a breast cancer claim for Evista. AstraZeneca's Nolvadex (tamoxifen) is approved for reducing the risk of breast cancer.

The information alleges much of the same conduct that AstraZeneca complained of in its Lanham Act suit - that Lilly executed its conduct using a number of tactics, including:

- One-on-one sales pitches by sales representatives promoting Evista to physicians about off-label uses of Evista. Sales representatives were trained to prompt or bait questions by doctors in order to promote Evista for unapproved uses;
- Encouraging sales representatives promoting Evista to send unsolicited medical letters to promote the drug for an unapproved use to doctors on their sales routes;
- Organizing a "market research summit" during which Evista was discussed with physicians for unapproved uses, including reducing the risk of breast cancer; and
- Creating and distributing to sales representatives an "Evista Best Practices" videotape, in which a sales representative states that "Evista truly is the best drug for the prevention of all these diseases" referring to osteoporosis, breast cancer, and cardiovascular disease.

The Lilly Consent Decree

The complaint for permanent injunction alleges that Lilly executed its illegal conduct using a number of additional tactics, including organizing "consultant meetings" for physicians during which unapproved uses of Evista were discussed; and calculating the incremental new prescriptions for doctors who attended Evista advisory board meetings in 1998 where unapproved uses for Evista were discussed. The consent decree imposes a broad range of obligations on Lilly, similar to a CIA. Among the other duties, Lilly must implement effective training and supervision of its marketing and sales staff for Evista and ensure that any future off-label marketing conduct is detected and corrected. Lilly agreed to be permanently enjoined from directly or indirectly promoting Evista for any unapproved use. Lilly further agreed to hire and use an independent review organization (IRO) to assess and evaluate its policies and procedures for the promotion of Evista and for its compliance with the consent decree. Unlike the Serono CIA, however, almost all of the obligations under the Consent Decree are limited to the promotion of a single drug, Evista.

Importantly, the consent decree obligates the company to submit to the government all market research conducted by or for the Evista Brand Team or Lilly Market Research to measure physician recall of marketing messages by Lilly sales representative for Evista, along with any summaries, reports, or presentations of such data. The consent decree also includes a provision obligating the company to obtain quarterly information on the interaction between their sales reps and physicians and provide it to the government.

Observations from Serono & Lilly

The Serono settlement confirms that the government will vigorously prosecute anti-kickback cases. In fact, the presence of the kickback element in the Serono case appears to be the major differentiation in the conduct alleged the Serono and Lilly charging documents.

From the perspective of compliance with the FDCA, both cases demonstrate that the government will not only prosecute promotion of unapproved drugs (or promotion of approved drugs for unapproved uses), but will thoroughly examine marketing efforts such as Serono's efforts to alter a diagnostic method to convince physicians to use a drug in a wider patient population and Lilly's promotional activities couched as "market research." It also signals that the government continues to closely scrutinize those activities considered "non-promotional" such as support for medical education and responses to unsolicited requests for information. A component of any post-approval advertising promotion compliance program should be a thorough corporate understanding of the labeling negotiations between the company and FDA.

Finally, the Serono case is the first known instance where the government has asked a company to evaluate or assess incentive compensation. And, the Lilly case is the first in which the government has addressed market research as a potential promotional tool. Both settlements demonstrate that the government continues to learn about the methods companies use to promote drugs and will continue to apply that knowledge to other companies as they come under investigation. It behooves those of us seeking to counsel or defend companies to do likewise.

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