Second Circuit Finds Prohibition on Off-Label Marketing Under the FDCA Violates the First Amendment

The Second Circuit handed down a landmark decision earlier this week on the issue of free speech rights in the context of the promotion of pharmaceutical products—a decision that has the potential to significantly impact how the Department of Justice (DOJ) investigates and prosecutes off-label promotion cases in the future. In *US v. Caronia*, No. 09-5006-cr, 2012 WL 5992141 (2d Cir. Dec. 3, 2012), the Court, in a 2-1 decision, vacated the conviction of Alfred Caronia, a pharmaceutical sales representative found guilty of conspiring to introduce a misbranded drug into commerce in violation of the Food, Drug and Cosmetic Act (FDCA), finding that his conviction, premised solely on his promotion of the drug Xyrem for off-label use, violated his free speech rights under the First Amendment.

The Decision

Caronia was hired as a Specialty Sales Consultant by Orphan Medical, Inc. (later acquired by Jazz Pharmaceutical) in March 2005 to promote Xyrem, a drug that was approved to treat patients with narcolepsy and which carried a black box warning. In late 2005, as part of a government investigation into the company's off-label promotion of Xyrem, Caronia was recorded on two occasions promoting the drug to a doctor for unapproved uses, such as insomnia, restless leg syndrome and fibromyalgia. Caronia was subsequently indicted and charged with conspiracy to introduce a misbranded drug into interstate commerce and introducing a misbranded drug into interstate commerce, both in violation of the FDCA. A jury found Caronia guilty of the first charge, but not the second. After sentencing, Caronia appealed the verdict, arguing that the misbranding provisions of the FDCA unconstitutionally restrict free speech and that the First Amendment does not permit the government to bar a pharmaceutical manufacturer and its representatives from providing truthful and non-misleading information about off-label uses of an FDA-approved drug.

In its holding, the Second Circuit found that the prosecution of Caronia was premised only on his speech in the form of his promotion of Xyrem. Although the government had argued on appeal that "Caronia's off-label promotion was used only as evidence of intent in this case," and thus, that the First Amendment was not implicated, the Court found that this argument was belied by the way the government tried the case. Specifically, the Court found that the government had argued at trial that Caronia's crimes derived specifically from his off-label promotion of Xyrem, without representing that such promotion was merely reflective of "intent." This, the Court concluded, left the jury to believe that Caronia's speech itself was the conduct at issue, thus implicating the First Amendment. The Court did not address what evidence besides speech could be offered to establish intended use, noting that "that is not what happened in this case," and therefore not deciding the issue.

In assessing Caronia's conviction under the First Amendment, the Second Circuit relied on the Supreme Court's decision in *Sorrell v. IMS Health, Inc.*, 131 S. Ct. 2653 (2011), in which the Supreme Court struck down on First Amendment grounds a Vermont law that prohibited pharmaceutical companies from using prescriber-identifying information for marketing purposes. In that case, the Supreme Court held that because the Vermont law imposed content- and speaker-based restrictions, it was subject to heightened scrutiny. The Supreme Court had then considered whether the government had proven that the restrictions on speech imposed by the law were consistent with the First Amendment under a heightened scrutiny analysis, invoking the four-part test set forth in *Central Hudson Gas & Electric Corp. v. Public Service Commission of New York*, 447 U.S. 557, 100 S. Ct. 2343 (1980).

Applying the Supreme Court's analysis to this case, the Second Circuit first found that, like the Vermont law at issue in *Sorrell*, the government's construction of the FDCA to prohibit off-label promotion by pharmaceutical manufacturers was content-based speech, in that speech about FDA-approved uses of a drug was permissible, while speech about off-label uses was not. Next, it found that the government was imposing speaker-based restrictions on speech, in that it targeted only one type of speaker—pharmaceutical manufacturers—and allowed others, such as physicians or academics, to speak without

restriction. Therefore, it held that the government's construction of the FDCA to prohibit off-label promotion was subject to heightened scrutiny.

Turning to the *Central Hudson* four-part test, the Second Circuit found that the first prong, which required that the speech at issue concern lawful activity and not be misleading, was met, in that the off-label use of a drug is lawful, and "the promotion of off-label drug use is not in and of itself false or misleading." Importantly, the Court noted that "off-label promotion that is false or misleading is not entitled to First Amendment protection."

Next, it found that the second prong of the *Central Hudson* test, requiring that the asserted government interest be substantial, was met, because the government's interests in drug safety and protecting the public health, by ensuring the integrity of the drug approval process and reducing patient exposure to drugs that are ineffective or unsafe, are substantial.

The Court then found, however, that the third prong of the *Central Hudson* test, which requires that the regulation at issue directly advance the governmental interest asserted, was not met. Specifically, it found that prohibiting the truthful off-label promotion of a drug "does not directly advance [the government's] interest in reducing patient exposure to off-label drugs or in preserving the efficacy of the FDA drug approval process because the off-label use of such drugs continues to be generally lawful." In that regard, it also found that such prohibitions interfered with physicians' and the public's access to pertinent information about drugs and could inhibit the making of informed treatment decisions.

Finally, the Court found that the fourth prong of the *Central Hudson* test, which required that the regulation at issue be narrowly drawn and not more extensive than necessary to serve the government's interest, was also not met. Here, the Court found that the ban on off-label promotion "is more extensive than necessary" to accomplish the government's interests and that "[n]umerous, less speech-restrictive alternatives are available." In short, it held that the government's asserted interests "could be served equally well by more limited and targeted restrictions on speech."

In closing, the Court stated: "We construe the misbranding provisions of the FDCA as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs." It concluded that the government "cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label use of an FDA-approved drug."

Circuit Judge Debra Ann Livingston issued a strong dissent, finding that the government had, in fact, presented Caronia's speech as evidence of intent, which the First Amendment does not prohibit. She then concluded that even if the speech at issue in this case were subject to a First Amendment analysis, she would uphold Caronia's conviction, because the government's application of the FDCA "directly advances a substantial government interest and is narrowly drawn to further that interest." Specifically, she stated that if pharmaceutical manufacturers were permitted to promote their products off-label, they would have little incentive to obtain FDA approval for those uses. She also stated that none of the less restrictive alternatives enumerated in the majority's opinion would be as effective in achieving the government's interest in preserving the integrity of the FDA approval process as prohibiting off-label promotion by pharmaceutical manufacturers.

Analysis

This decision is a sharp rebuke to the government's approach to bringing off-label cases under the FDCA, which in recent years has involved prosecuting dozens of off-label cases through which the government has collected billions of dollars in settlements with drug manufacturers. In addition, the concept that truthful, non-misleading speech about off-label uses of a drug is protected by the First Amendment is likely to have implications in a variety of other types of cases. For example, the holding in this case undermines the theory set forth in civil off-label cases brought under the False Claims Act (FCA), where the government has argued that a company's off-label promotion in and of itself causes false claims to be submitted to the federal healthcare programs. Although this is a landmark decision, however, the holding here is unlikely to completely deter the government from bringing future off-label cases.

Most significantly, the holding applies only to the *truthful*, *non-misleading* off-label promotion of pharmaceutical products. Because *Caronia* does not afford protection for false or misleading promotional messages, those could continue to be prosecuted under the FDCA. This will likely lead the government to characterize its future off-label investigations and prosecutions as involving false and misleading conduct (e.g., whether the manufacturer overstated efficacy or minimized safety issues) and lead to spirited counterarguments from targeted companies that promotional messages were truthful and not misleading. That debate is evident in *Caronia*—the majority presumed that Caronia's promotion was truthful and non-misleading, while the dissent noted that Caronia told the doctor that Xyrem—which carries a black box warning—was a "'very safe drug' with no contraindications." In practice, what constitutes truthful and non-misleading off-label promotion in future cases will be difficult to define, given that the court articulated no standard for what makes an off-label claim truthful and non-misleading.

Of note, the Court also did not decide the issue of whether the government could offer other evidence of off-label promotion to establish intended use, leaving open the possibility that such evidence could be used in a future prosecution.

Rather than deterring the government from prosecuting off-label cases, realistically, this decision may only serve to change its approach. The decision will likely impact the types of cases the government chooses to bring, forcing it to focus on cases where the allegations at issue involve demonstrably false statements by manufacturers in promoting off-label uses of a drug. And of course, the holding in this case would not apply to kickback-related allegations brought under the FCA, where the issue is whether physicians were paid or provided items of value with the intent to induce them to prescribe a product, resulting in a false claim. Therefore, in the cases that the government does choose to prosecute, it is likely to focus more on allegations that a company's off-label promotion involved false or misleading statements or that it paid kickbacks to physicians to induce prescriptions of a product.

Perhaps the most important result of *Caronia* will be the lessons that the government draws from it. Although it is likely that the government at least will seek rehearing *en banc* of the decision, given its importance and the 2-1 split, the facts are not good for the government with respect to the way in which the case was presented at trial. It has also been less than two years since the Supreme Court decided *Sorrell*, and the writing may be on the wall as to the Court's attitude on the commercial speech doctrine. This result, however, may present an opportunity for the FDA and the DOJ to develop a sensible policy to guide company conduct regarding off-label promotion, given the clash between free speech rights in this context and the misbranding statutes.

The majority's holding in *Caronia* will soon be considered by other Circuit courts. Indeed, on December 6, 2012, the Ninth Circuit heard arguments by W. Scott Harkonen, who was convicted of wire fraud regarding statements in a news release reporting on the results of a clinical study, that his conviction violated his free speech rights.

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