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Second Circuit Rules Off-Label Marketing is Protected by First Amendment

On December 3, 2012, the United States Court of Appeals for the Second Circuit, in a 2-1 opinion, vacated the criminal conviction of a pharmaceutical sales representative for promoting off-label uses of a particular drug. Rejecting the government's theory, the court held "***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.***"

While the opinion only binds states within the Second Circuit's jurisdiction (New York, Connecticut, and Vermont), the decision potentially has far-reaching effects on future FDA litigation strategies and False Claims Act prosecutions.

A. Background

The federal Food, Drug, and Cosmetic Act ("FDCA") provides that FDA must approve a drug for specific uses before it can be sold in interstate commerce.[1] To obtain FDA approval, a manufacturer must demonstrate, through clinical trials, the drug's safety and effectiveness for each intended use.[2] However, once approved for any use, the drug may be prescribed by physicians for both FDA-approved and unapproved ("off-label") uses.[3]

The FDCA deems a drug "misbranded" when, among other things, its labeling lacks "directions under which the layperson can use a drug safely and for the purposes for which it is intended."[4] It is FDA's position, and courts have held, that oral or written statements by manufacturers or their representatives may be used to demonstrate the manufacturer is promoting, and has established, an intended use that is an off-label, or unapproved, use of its product. Recently, the government has gained major settlements from leading pharmaceutical companies for False Claims Act violations based on allegations of off-label promotion.

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[1] 21 U.S.C. § 355(a).
[2] 21 U.S.C. § 355(d).
[3] *See Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 350 (2001).
[4] *See* 21 U.S.C. § 352(f); 21 C.F.R. § 201.5.

In *U.S. v. Caronia*, Orphan Medical – now Jazz Pharmaceuticals – hired Alfred Caronia as a pharmaceutical sales representative for a drug called Xyrem. Tape recordings produced during an FDA sting operation revealed Caronia had been promoting Xyrem for off-label uses. He was subsequently tried under FDCA's misbranding provisions and appealed his conviction to the Second Circuit.

B. Second Circuit Decision

1. Majority Decision

The majority held that the FDCA does not criminalize mere off-label promotion. While the FDCA addresses misbranding, it does not expressly prohibit the "promotion" or "marketing" of drugs for off-label use. FDA interprets the FDCA and provides in its regulations that such promotion is evidence of a drug's intended use rather than a per se violation. Therefore, applying the principle of constitutional avoidance, the majority interpreted the FDCA as not criminalizing off-label promotion, in and of itself, so as to avoid First Amendment concerns with the statute.

The majority rejected the government's argument that the First Amendment was not implicated by Caronia's off-label promotion. The government argued that Caronia's statements played only an evidentiary role in determining Xyrem's intended use. The majority disagreed, finding that both the government and district court gave the jury the impression that Caronia's speech itself was the proscribed conduct.

The majority also rejected what it described as the government's interpretation of FDCA's misbranding provisions to prohibit off-label promotion. This analysis relied heavily on the Supreme Court's opinion last year in *Sorrell v. IMS Health*.[5] Following *Sorrell*'s roadmap, the *Caronia* majority engaged in a two-step inquiry, first determining whether the regulation was "content-" and "speaker-based," and second, determining whether the restriction passed constitutional muster under a "heightened level of scrutiny."

In step one, the majority found that the government's construction of the FDCA's misbranding provisions was both "content" and "speaker-based." It was content-based because it permitted speech about "government-approved" uses of prescription drugs, while prohibiting truthful speech about off-label uses that doctors might find useful. The government's construction was speaker-based because it targets only one kind of speaker – pharmaceutical manufacturers – while allowing all others to speak without restriction.

Proceeding to step two, the court examined the government's interpretation under heightened scrutiny. The Second Circuit did not decide the exact level of scrutiny to be applied. Instead, it held the interpretation was unconstitutional even under the less-stringent *Central Hudson* test. The

[5] 131 S. Ct. 2653 (2011).

Supreme Court established this four-part test in a prior case out to determine whether commercial speech is protected by the First Amendment. [6] According to the test: (1) the speech must not be misleading and must concern lawful activity; (2) the asserted government interest must be substantial; (3) the regulation must directly advance the governmental interest asserted; and (4) the regulation must be "narrowly drawn," and may not be more extensive than necessary to serve the interest.

Although easily satisfying prongs one and two, the majority held that the government's interpretation of the FDCA misbranding provisions failed both prongs three and four. The majority found that the interpretation did not directly advance the government's interest in drug safety because off-label drug use is not unlawful. It further found that prohibiting off-label promotion while allowing off-label use interferes with the free flow of relevant treatment information and could actually be to the public's detriment.

The majority found the interpretation did not satisfy the fourth prong because a complete and criminal ban on off-label promotion was more extensive than necessary to achieve the government's interest in promoting the effectiveness of the drug approval process. The court listed several alternative means, such as further developing its warning or disclaimer systems, adding safety tiers to help distinguish between drugs, requiring pharmaceutical companies to list all applicable or intended indications when they first apply for FDA approval, imposing ceilings on off-label prescriptions, or, where off-label use is "exceptionally concerning," banning off-label use altogether.

Failing parts three and four of *Central Hudson*, the majority determined the FDCA does not criminalize truthful off-label promotion of an FDA-approved drug. Accordingly, Mr. Caronia's conviction under FDCA's misbranding provisions was vacated.

2. Judge Livingston's Dissent

The lone dissenting judge, Judge Debra Ann Livingston, vigorously disagreed, arguing that, by vacating the conviction, "the majority calls into question the very foundations of our century-old system of drug regulation." Judge Livingston reasoned that, if drug companies were allowed to engage in off-label promotion, they would have little incentive to seek FDA approval for those off-label uses. The dissent then performed its own analysis of the FDCA misbranding provisions and concluded that they withstood scrutiny under the Supreme Court decisions in *Central Hudson* and *Sorrell*.

[6] *Central Hudson Gas & Electric Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557 (1980).

C. Implications of the Decision

At this point, the practical implications for the regulated industry cannot be foretold. Given the 2-to-1 decision with a vigorous dissent on an issue of great importance, FDA is likely to seek a rehearing *en banc* by the Circuit and/or Supreme Court review. Unless and until the decision is overturned, however, it will be cited against the government by a wide range of FDA-regulated companies – in the pharmaceutical, medical device, biotechnology, and food and dietary supplement industries – who engage in marketing and promotion of their FDA-regulated products.

The decision may cause FDA and the Department of Justice to be more cautious in using criminal sanctions to address off-label promotion and in bringing cases involving truthful rather than false or misleading information. While FDA may ultimately consider the Second Circuit's advice and adopt new regulations concerning off-label promotion, this is unlikely in the absence of further judicial set-backs.

It will be important to consider how this decision may affect settlements of False Claims Act (FCA) cases against the pharmaceutical industry based on off-label promotion. In recent years, the government has recovered billions in settlements with various major pharmaceutical companies. In those cases, the government asserted that, when a drug company engages in off-label promotion, and if federal funds have been paid (through Medicare, for example) for these promoted non-approved uses, the government has received and paid "false claims" for which the government is entitled to civil penalties plus treble damages.[7] Given the Second Circuit's ruling that truthful off-label promotion is constitutionally permissible under the FDCA, the government's theory of liability under the FCA will be called into question.

If you have any questions regarding this client alert or the court's decision, feel free to contact any of the authors.

[7] 31 U.S.C. § 3729.