Second Circuit Overturns Off-Label Marketing Conviction On First Amendment Grounds

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Applying the First Amendment in a way that could significantly alter the prosecutorial and regulatory landscape in Food and Drug cases, the United States Court of Appeals for the Second Circuit has overturned the conviction of a pharmaceutical sales representative for conspiring to introduce a misbranded drug into interstate commerce, where his prosecution and conviction were based on conversations he had with physicians about off-label uses for an approved drug. In *United States v. Caronia* (Dkt. No. 09-5006 cr, December 3, 2012), a 2-1 decision, the Second Circuit held 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." This is a major victory for pharmaceutical manufacturers, who have been under government scrutiny for off-label marketing practices for several years.

This Client Advisory will analyze the *Caronia* decision and discuss its implications for pharmaceutical companies.

Facts

Orphan Medical, Inc., now known as Jazz Pharmaceutical, manufactured a drug called Xyrem. Xyrem's active ingredient is gamma-hydroxybutryate ("GHB"), also known as the "date rape" drug. In July 2002, the FDA approved Xyrem to treat narcolepsy patients who experience cataplexy, a condition associated with weak or paralyzed muscles. In November 2005, the FDA approved Xyrem to treat narcolepsy patients with excessive daytime sleepiness ("EDS"). Because of Xyrem's profound side effects, when it approved the drug in 2002, the FDA required a "black box" warning which stated, among other things, that Xyrem had not been proven to be safe and effective in patients under 16 years of age and that it had limited experience in elderly patients.

In March 2005 Orphan hired Alfred Caronia as a Specialty Sales Consultant to promote Xyrem. In July 2005, Caronia instituted a speaker's program for Xyrem. Through the speaker's program, Orphan paid physicians to speak to other physicians about Xyrem's approved uses. Pursuant to Orphan policy, if a physician asked Caronia about unapproved uses for Xyrem, Caronia was required to complete a "medical information request form," and Orphan would deal with the physician's request. On the other hand, if a physician hired to speak at a program was asked about unapproved uses, he or she was free to answer such questions.

In the Spring of 2005 the government began to investigate Caronia and Dr. Peter Gleason, a speaker hired by Caronia, regarding alleged off-label marketing of Xyrem. Caronia was heard on two consensual tape recordings promoting Xyrem to physicians for unapproved uses. On July 25, 2007,

Caronia was indicted, and on August 18, 2008, the government filed a superseding information. The superseding information consisted of two misdemeanor counts. Count One accused Caronia of conspiring to introduce a misbranded drug into interstate commerce in violation of 21 U.S.C. §§ 331(a) and 333(a)(2). Count Two accused him of introducing a misbranded drug into interstate commerce, in violation of 21 U.S.C. §§ 331(a) and 333(a)(2). Count One alleged two conspiratorial objects. First, it alleged that Caronia and others conspired to introduce Xyrem and cause the introduction of Xyrem into interstate commerce when Xyrem was misbranded. Second, the information alleged that Caronia and his coconspirators "marketed Xyrem for medical indications that were not approved by [the] FDA when, as [they] . . . well knew and believed, Xyrem's labeling lacked adequate directions for and warnings against such uses, where such uses could be dangerous to the user's health." This second object also formed the basis for the allegations in Count Two.

After trial, the jury found Caronia guilty of Count One, specifically with respect to the first object, the conspiracy to introduce Xyrem into interstate commerce when it was misbranded. The jury acquitted Caronia of the second prong of Count One, and also of Count Two.

The Court's Decision

On appeal, Caronia argued that the FDCA's misbranding provisions prohibit off-label promotion and thus violate the First Amendment's free speech protections. The Second Circuit agreed, albeit on somewhat narrower grounds. It found that the FDCA did not criminalize off-label promotion itself, but rather, viewed off-label promotion as evidence of misbranding. However, the Court found that the government had, indeed, prosecuted Caronia for off-label promotion and that the District Court had instructed the jury that it could convict on that theory. Under those circumstances, the Second Circuit held, Caronia's conviction must be vacated.

Writing for the majority, Judge Denny Chin began by rejecting the government's argument that at trial it did not prosecute Caronia for off-label promotion, but that it presented Caronia's off-label promotion merely as evidence of an agreement to engage in product mislabeling. To the contrary, Judge Chin wrote, the record revealed that "the government repeatedly argued that Caronia engaged in criminal conduct by promoting and marketing the off-label use of Xyrem." Further, Judge Chin wrote, "[t]he government never argued in summation or rebuttal that the promotion was evidence of intent. . .[and] the government never suggested that Caronia engaged in any form of misbranding other than the promotion of the off-label use of an FDA-approved drug." Further, Judge Chin stated, the trial court's instruction left the jury with the impression that it could convict Caronia for having engaged in off-label promotion – that is, for his commercially related speech.

Having found that the government had prosecuted Caronia for commercial speech, Judge Chin then addressed the level of scrutiny to be used in determining whether that speech was protected under the First Amendment. Judge Chin looked chiefly to two Supreme Court decisions: *Sorrell v. IMS Health, Inc.*, 131 S. Ct. 2653 (2011), and *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of N.Y.*, 447 U.S. 557 (1980). In *Sorrell,* the Supreme Court struck down a Vermont law which made it illegal for pharmacies, health insurers and similar entities to sell prescriber information, or for pharmaceutical companies to use such information for a commercial purpose, without the prescriber's consent. The Court found that the law imposed both content and speaker-based restrictions on commercial speech, and was thus subject to heightened, though unspecified, scrutiny. Under that heightened scrutiny, the Court concluded, the Vermont law failed to pass constitutional muster.

Judge Chin wrote that the restrictions imposed on discussions of off-label use were both content and

speaker-based. The restrictions were content-based because they permitted discussions of government-approved uses for approved drugs but prohibited discussions of non-approved uses of those drugs, even though off-label use is itself legal. The restrictions were speaker-based, in that it specifically prohibited manufacturers from discussing off-label uses, while permitting others, such as prescribing physicians, to discuss those same uses.

Sorrell, and in turn the Second Circuit in *Caronia*, relied on the four-part test established in *Central Hudson* to determine whether commercial speech is protected by the First Amendment. As stated in *Central Hudson*, that test is as follows:

At the outset, we must determine whether the expression is protected by the First Amendment. For commercial speech to come within that provision, it at least must concern lawful activity and not be misleading. Next, we ask whether the asserted governmental interest is substantial. If both inquiries yield positive answers, we must determine whether the regulation directly advances the governmental interest asserted, and whether it is not more extensive than is necessary to serve that interest.

Judge Chin found that the first two criteria were "easily satisfied," since the commercial speech in question concerned lawful activity and the government has a substantial interest in maintaining the integrity of the drug approval process. However, the prohibition against off-label promotion failed to satisfy the third criterion, in that it did not directly advance the governmental interest asserted. Judge Chin explained that since "off-label drug use itself is not prohibited, it does not follow that prohibiting the truthful promotion of off-label drug usage by a particular class of speakers would directly further the government's goals of preserving the efficacy and integrity of the FDA's drug approval process and reducing patient exposure to unsafe and ineffective drugs." Moreover, he wrote, prohibiting off-label marketing "'paternalistically' interferes with the ability of physicians and patients to receive potentially relevant treatment information; such barriers to information about off-label use could inhibit, to the public's detriment, informed and intelligent treatment decisions."

The Second Circuit also found that prohibiting off-label marketing failed under the fourth criteria, in that it was more extensive than necessary to achieve the government's purpose. Judge Chin listed a panoply of alternative ways to regulate off-label usage, such as full disclosure of all intended uses on new drug applications, caps on the number of prescriptions would be permitted for off-label uses, or, for certain types of drugs, outright bans on off-label uses.

Judge Chin's majority opinion closed by stating:

We construe the misbranding provisions of the FDCA as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs. Our conclusion is limited to FDA-approved drugs for which off-label use is not prohibited, and we do not hold, of course, that the FDA cannot regulate the marketing of prescription drugs. We conclude simply 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.

Judge Debra Ann Livingston wrote a dissent (notably, Judge Livingston also wrote a dissenting opinion when the Second Circuit decided *Sorrel*; it was the Second Circuit's decision which the Supreme Court later affirmed). Judge Livingston agreed with the government that it did not prosecute Caronia for his speech, but rather, in keeping with *Wisconsin v. Mitchell*, 508 U.S. 476, 489 (1993), relied on his speech as evidence of his intent to engage in a mislabeling conspiracy.

What Can We Expect?

The Second Circuit's *Caronia* decision could drastically change how the FDA and DOJ enforce the

FDCA's misbranding provisions. Just a simple Wikipedia search reveals at least 23 off-label marketing settlements having occurred since 2004. The government has reaped billions of dollars in civil and criminal fines and penalties from these settlements. It seems certain that the government will move for reargument and seek *en banc* review, and, failing that, will petition the Supreme Court for *certiorari*. There is a very good chance that the Supreme Court will agree to take on *Caronia*, since it is a natural outgrowth of its decision in *Sorrell*. Thus, while for now *Caronia* is a substantial victory for pharmaceutical companies in at least three states ((New York, Connecticut, and Vermont, which comprise the Second Circuit), it is likely that the final chapter has not yet been written.