Second Circuit Holds First Amendment Bars Conviction Based Solely on Off-Label Promotion of FDA-Approved Drug

In its long-awaited decision in *United States v. Caronia*, the Second Circuit ruled today that the First Amendment bars the criminal prosecution of pharmaceutical manufacturers or their sales representatives for truthful, non-misleading speech promoting the lawful, off-label use of an FDA-approved drug. By a vote of two-to-one, the panel vacated the conviction of a pharmaceutical sales representative for conspiracy to introduce a misbranded drug into interstate commerce in violation of the Food, Drug, and Cosmetic Act ("FDCA"). The Second Circuit recognized that criminalizing a drug manufacturer's speech about a drug's lawful, off-label use would violate the First Amendment; the court therefore construed the FDCA not to prohibit such speech. The majority did not decide whether, or to what extent, the First Amendment would allow the government to rely upon a pharmaceutical manufacturer's promotional statements regarding off-label uses as evidence of the drug's "intended use" in a prosecution for introducing a drug into commerce without "adequate instructions for use." The majority's analysis calls into serious doubt, however, the government's ability to prosecute a misbranding charge based on off-label promotion or, more broadly, to rely upon a drug manufacturer's dissemination of truthful, non-misleading information about a drug's off-label uses in such a prosecution. A copy of the court's decision can be found here.

The key features of today's holding are:

- The FDCA's misbranding provisions do not prohibit the truthful off-label promotion of FDA-approved prescription drugs.
- If the FDCA did criminalize the truthful promotion of a drug's lawful, off-label use by pharmaceutical manufacturers and their representatives, it would violate the First Amendment.
- The panel addressed only the government's ability to prosecute off-label promotional speech itself, and did not resolve whether the government could rely on promotional speech about off-label uses as evidence of a drug's "intended use." However, the court's First Amendment analysis – including its dismissal of the government's "paternalistic" interest in interfering with doctors receiving potentially relevant treatment information and its emphasis on less speech-restrictive alternatives to FDA's current regime – will have broader applications.
- Although the decision arose from a criminal prosecution, it will have implications as well for other enforcement activities, including False Claims Act suits, in which the government or relators urge off-label promotion as a basis for liability.

Under the FDCA, a drug must bear on its labeling "adequate directions for use," which the Food and Drug Administration ("FDA") construes as requiring that a drug's labeling give directions adequate "for the purposes for which it is intended." A drug that lacks such instructions is misbranded, and introducing a misbranded drug into interstate commerce is a criminal offense. The panel majority observed that, although the FDA's implementing regulations "do not expressly prohibit the 'promotion' or 'marketing' of drugs for off-label use," the Department of Justice has long construed them in that fashion, and that the "government has repeatedly prosecuted – and obtained convictions against – pharmaceutical companies and their representatives for misbranding based on their off-label promotion."

The defendant, Alfred Caronia, was convicted of conspiring to introduce a misbranded drug into commerce based on his speech about an off-label use of the drug. Caronia was a sales representative for Jazz Pharmaceuticals, and in October and November 2005, a government informant twice recorded Caronia on

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audio tape promoting the drug Xyrem (which was FDA approved only for treating certain types of narcolepsy symptoms) "for unapproved uses, including unapproved indications and unapproved subpopulations." Caronia was subsequently charged with having conspired to introduce a misbranded drug (Xyrem) into commerce. Caronia moved to dismiss the charges on First Amendment grounds, but the district court denied the motion. The district court instructed the jury that Caronia was "not permitted to promote uses for [Xyrem] that [had] not been cleared" by the FDA. The jury convicted Caronia of the conspiracy charge, and the district court sentenced him to one year of probation and 100 hours of community service. On appeal, Caronia renewed his First Amendment challenge, and Ropes & Gray filed an amicus brief urging that the government's prosecution of Caronia on the basis of his speech under an ambiguous FDA regulatory regime violated the First Amendment.

The Second Circuit agreed that the First Amendment would not permit the government to convict a pharmaceutical manufacturer or its sales representative solely on the basis of promoting off-label uses, and so it construed the FDCA not to prohibit such speech. Whereas the government contended, and the dissenting judge agreed, that Caronia's speech about off-label uses had only been used as "evidence" of the drug's "intended use," the panel majority rejected that interpretation of the district court proceedings. The court pointed out that the government had "repeatedly argued" at trial that "Caronia engaged in criminal conduct by promoting and marketing the off-label use of Xyrem," had "never argued in summation or rebuttal that the promotion was [merely] evidence of intent," and had "never suggested that Caronia engaged in any form of misbranding other than the promotion of the off-label use of" Xyrem. The trial record made "clear that the government prosecuted Caronia *for* his promotion and marketing efforts." Thus, the majority reasoned that it did not need to decide whether the First Amendment "permits the government to prove intended use by reference to promotional statements made by drug manufacturers or their representatives."

Although the Second Circuit did not directly opine on whether promotion of off-label uses could be relied upon as evidence of the crime of introducing a misbranded drug, the majority's First Amendment analysis of the prosecution of Caronia based on off-label speech alone raises serious questions whether a prosecution in which off-label promotion is relied on as "evidence" of a misbranding crime would be constitutionally permissible. The majority stressed that the FDA's restrictions on off-label speech by drug manufacturers constituted a content- and speaker-based limitation that required the court to apply heightened scrutiny. Citing the Supreme Court's recent decision in *Sorrell v. IMS Health, Inc.*, which struck down a restriction against pharmaceutical companies relying on doctor prescribing patterns to target their promotional communications, the majority noted that "a claim to First Amendment protection here is more compelling than in *Sorrell* because this case involves a criminal regulatory scheme subject to more careful scrutiny." The majority also stressed the importance to patient health of the information that pharmaceutical companies can communicate to doctors, and the irony that others could speak freely of lawful off-label uses, while manufacturers, who often have the best information, are silenced. "[P]rohibiting off-label promotion by a pharmaceutical manufacturer while simultaneously allowing off-label use '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." Because the off-label use was lawful, and other speakers remain free to advocate such use, the panel concluded that the FDA's ban on off-label promotion by manufacturers "does not directly advance its interest in … preserving the efficacy of the FDA drug approval process." Finally, the panel stressed that "[n]umerous, less speech-restrictive alternatives are available" to the government, including directly regulating off-label uses, focusing on misleading information, or developing a system of disclaimers or even different safety tiers among off-label uses. These points would seem to be equally applicable to the government's use of off-label promotional statements as "evidence" of a violation of the FDCA's misbranding provisions.

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Although the Second Circuit's decision arises in the context of a criminal prosecution, it will provide helpful support to pharmaceutical manufacturers in other contexts as well where the government seeks to enforce the FDCA based on alleged off-label promotion. For example, the panel's narrowing construction of the FDCA would limit the Inspector General's application of the exclusion remedy to pharmaceutical companies in prosecutions alleging off-label promotion as well as the government and relators' ability to rely on allegations of off-label promotion as the basis for asserting liability under the False Claims Act. If you have further questions about the implications of the *Caronia* decision, please consult your usual Ropes & Gray advisor.

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