Landmark Second Circuit Decision Strikes Down Criminal Prohibition Against Truthful and Non-Misleading Off-Label Communications By Pharmaceutical Companies

On December 3, 2012, the U.S. Court of Appeals for the Second Circuit issued its long-anticipated decision in *United States v. Caronia*, No. 09-5006-cr. In a 2-1 opinion authored by Judge Denny Chin, the court held that construing the Federal Food, Drug, and Cosmetic Act (FDCA) and its implementing regulations to prohibit pharmaceutical companies from engaging in truthful and non-misleading speech regarding unapproved or "off-label" uses of Food and Drug Administration (FDA) approved drugs violates the First Amendment. The Second Circuit applied the First Amendment analysis set forth in *Sorrell v. IMS Health Inc.*,[1] a case that Arnold & Porter handled at the trial and appellate stages, including the petition and merits phases in the U.S. Supreme Court. The *Caronia* court explained that FDCA prosecutions premised on off-label promotion impermissibly discriminate against pharmaceutical companies based on the content of their speech. Anyone other than pharmaceutical companies, even individuals or entities outside the healthcare field, may freely discuss off-label uses of approved drugs. Yet, under the government's theory of prosecution, the same speech becomes criminal when uttered by pharmaceutical companies – entities who arguably are the most knowledgeable about the drugs under discussion.

The *Caronia* court ruled that this restriction on the free flow of information not only fails to advance directly the government's substantial interests in drug safety and public health, but also is far more restrictive of protected speech than necessary to achieve the government's stated ends. Because the First Amendment bars the government from prohibiting pharmaceutical companies from engaging in truthful and non-misleading speech about off-label uses, the Second Circuit interpreted the FDCA not to prohibit this speech. This landmark ruling calls into question the core prosecutorial theory used by the government to bring criminal enforcement actions for off-label promotion under FDA's "intended use" regulations and may also limit the ability of the government and private plaintiffs to argue that off-label promotion leads to the submission of false claims.

1 131 S. Ct. 2653 (2011).

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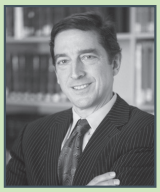

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Background

At the center of *Caronia* is the promotion of prescription drugs for "off-label" use. Under the FDCA, pharmaceutical manufacturers may not distribute prescription drugs in interstate commerce without first obtaining FDA approval. Although FDA approves drugs for specific indications, physicians generally are not limited by a drug's approved uses. They can and often do prescribe FDA-approved drugs for unapproved or off-label uses in the practice of medicine.

But under the government's interpretation of the FDCA and FDA's implementing regulations, pharmaceutical companies are restricted in their ability to speak to healthcare professionals about off-label uses of approved medicines. In particular, the FDCA prohibits distribution of a "misbranded" drug, a criminal offense, which occurs when, *inter alia*, a drug is promoted and shipped without "adequate directions for use."[2] FDA has defined "adequate directions" to mean "directions under which the layman can use a drug safely and for the purposes for which it is intended."[3] Further, according to FDA, the adequacy of a drug's directions for use depends on the "objective intent" of the pharmaceutical manufacturer.[4] The government long has posited that the misbranding provision requiring "adequate directions for use" blocks manufacturers from engaging in any speech about off-label uses, except in certain narrowly defined circumstances described by FDA in unpublished guidance.[5]

The District Court Proceedings

Caronia began in 2005 when the federal government launched an investigation into Orphan Medical, Inc. (Orphan), a wholly owned subsidiary of Jazz Pharmaceuticals, and its sale of Xyrem®, a central nervous system depressant. A few months earlier, Orphan hired Alfred Caronia and Dr. Peter Gleason to market Xyrem®. Although FDA had approved Xyrem® for two medical indications relating to narcolepsy patients – cataplexy and excessive daytime sleepiness – the government obtained two audio-recordings of Caronia and Gleason promoting Xyrem® to a physician for unapproved indications including insomnia and fibromyalgia and for unapproved patient populations including the elderly.[6]

Two years after the investigation began, Orphan pled guilty to felony misbranding and settled for US$20 million,[7] and Gleason pled guilty to misdemeanor misbranding.[8] Caronia, however, decided not to enter into a pretrial disposition. In a motion to dismiss, Caronia argued in part that the misbranding provisions as applied to him violated his speech rights under the First Amendment. "Reduced to its essence, Caronia's argument [was] that the government cannot restrict truthful, non-misleading promotion by a pharmaceutical manufacturer (or its employees) to a physician of the off-label uses of an FDA-approved drug."[9] The district court denied the motion, concluding that the government's interest in preserving drug integrity and safety justified the speech restriction under the intermediate scrutiny applicable to commercial speech.[10] After a ten-day trial, the jury found Caronia guilty of conspiracy to introduce a misbranded drug into interstate commerce.[11]

The Second Circuit, Following *Sorrell*, Reverses

While the case was on appeal to the Second Circuit, the Supreme Court issued its decision in *Sorrell*. There, the Court invalidated under the First Amendment a Vermont law that restricted pharmaceutical companies from using

2 21 U.S.C. §§ 331(a); 352(f).

3 *Id.*

4 21 C.F.R. §§ 201.5, 201.128.

5 FDA, Draft Guidance for Industry – Responding to Unsolicited Requests for Off-Label Information about Prescription Drugs and Medical Devices (2011); Notice of Availability of Draft Guidance, 76 Fed. Reg. 82303-01 (Dec. 30, 2011); FDA, Guidance for Industry – Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (2009).

6 Slip op. at 11-16.

7 Press Release, U.S. Dep't of Justice, Jazz Pharmaceuticals, Inc. Agrees to Pay $20 Million to Resolve Criminal and Civil Allegations in "Off-Label" Marketing Investigation (July 13, 2007), http://www.justice.gov/usao/nye/pr/ 2007/2007jul13a.html.

8 *United States v. Caronia*, 576 F. Supp. 2d 385, 390 (E.D.N.Y. 2008).

9 *Id.* at 393.

10 *Id.* at 394-402.

11 Slip op. at 24.

prescriber-identifying data for marketing purposes.[12] It concluded that Vermont's law was subject to "heightened judicial scrutiny" because the law imposed both content- and speaker-based restrictions on the speech of only pharmaceutical companies.[13] In the end, however, the Court ruled that the law could not survive even the less stringent intermediate scrutiny under the four-part *Central Hudson* test.[14] Following the *Sorrell* decision, the Second Circuit in *Caronia* requested supplemental briefing regarding its impact on the issues presented by *Caronia*.

Before the Second Circuit, the government claimed that the FDCA did not prohibit off-label promotion itself. Instead, the government asserted - and Judge Debra Livingston in a 30-page dissent agreed - that such speech was merely "evidence" that a manufacturer's intended use of a drug was incompatible with the directions in its labeling, which by law are limited to approved uses.[15] The *Caronia* majority quickly disposed of this argument. Assuming without deciding that the evidentiary use of off-label speech in misbranding prosecutions falls outside the First Amendment, the Second Circuit explained that the government had used Caronia's off-label speech at trial for more than mere evidentiary purposes. The court stressed that the government's closing arguments alone referred to "Caronia's off-label promotion of Xyrem[®] *… over forty times*."[16] Likewise, the court added, the government's summation and the jury instructions "led the jury to believe that Caronia's promotional speech was, by itself, determinative of his guilt."[17] No matter how brazen Caronia's promotional efforts were,[18] as the court explained, Caronia's truthful off-label speech alone could not serve as the basis for prosecution.[19]

The Second Circuit next addressed the government's view that the FDCA could be construed, consistent with the First Amendment, to criminalize truthful off-label promotion by drug companies and their representatives. Closely tracking the Supreme Court's analysis in *Sorrell*, the Second Circuit reasoned that criminally prohibiting such truthful speech would impose presumptively invalid content- and speaker-based restrictions.[20] The court added that heightened scrutiny was even more appropriate than in *Sorrell*, because "this case involves a criminal regulatory scheme."[21]

Continuing to follow *Sorrell*, the Second Circuit explained that, although heightened scrutiny applied, prohibiting truthful off-label speech by drug manufacturers fails even intermediate scrutiny under *Central Hudson*. To pass that test, the court observed, (1) the speech at issue must be non-misleading and relate to lawful activity; (2) the government must have a substantial interest in regulating the speech; (3) the regulation must directly advance the government's asserted interest; and (4) the regulation must not impinge on any more speech than is necessary to achieve the governmental interest.[22] The *Caronia* court explained that off-label promotion is not inherently misleading, it concerns a lawful activity, and the government has substantial interests in "preserving the effectiveness and integrity of the FDCA's drug approval process, and … reducing patient exposure to unsafe and ineffective drugs."[23]

In a decision that could have broader consequences, the Second Circuit held that construing the FDCA to prohibit

12 *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653 (2011).

13 *Id.* at 2664.

14 *Id.* at 2667-72.

15 Slip op. at 27; *see also id.* at 13 (Livingston, J., dissenting) ("Consistent with the First Amendment, however, otherwise permissible conduct may become *impermissible* if undertaken with a prohibited motive, and speech may be used as evidence of such a motive.").

16 *Id.* at 28 (majority opinion) (emphasis added).

17 *Id.* at 30.

18 Excerpts of the audio recordings introduced at trial make clear that Caronia engaged in unequivocal off-label promotion. *See id.* at 15 (excerpt from October 26, 2005 recording in which Caronia recommends Xyrem® for fibromyalgia, periodic leg movement, restless leg, Parkinson's, and, in the future, multiple sclerosis).

19 *Id.* at 31 ("Here, the proscribed conduct for which Caronia was prosecuted was precisely his speech in aid of pharmaceutical marketing.").

20 *Id.* at 39-41.

21 Slip op. at 41.

22 *Id.* at 37-38.

23 *Id.* at 42-43.

truthful off-label promotion would not directly advance the government's interests; nor would it be the least-restrictive means available to achieve those interests. Because doctors lawfully write off-label prescriptions, the court did not see how proscribing truthful off-label communications by pharmaceutical companies furthered the government's interests in protecting public health. Indeed, mirroring the reasoning of *Sorrell*, the majority found that "prohibiting 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."[24] Moreover, the Second Circuit identified several ways in which the government could advance its interests without unduly restricting protected speech. Adopting a more robust system for warnings and disclaimers, requiring drug applications to include all intended uses, limiting the number of off-label prescriptions, or even prohibiting off-label prescriptions would all serve the government's interests "equally well" without impinging upon free speech.[25] The court rejected as "conclusory" and unsupported the government's reply that such alternatives were not feasible or effective.[26]

Applying the canon of constitutional avoidance, the Second Circuit construed the FDCA and its implementing regulations not to criminalize truthful off-label promotion. It accordingly vacated Caronia's conviction.[27]

24 *Id.* at 44.

25 *Id.* at 48-50.

26 *Id.* at 50-51. Judge Livingston disagreed with the majority's opinion that prohibiting off-label promotion is unconstitutionally paternalistic, concluding that the prohibition was the least restrictive way of advancing the government's interests in both drug safety and effectiveness. *Id.* at 21 (Livingston, J., dissenting) ("If drug manufacturers were allowed to promote FDA-approved drugs for non-approved uses, they would have little incentive to seek FDA approval for those uses. Prohibiting such promotion is thus 'one of the few mechanisms available' to encourage participation in the approval process."). In her view, the majority's decision "calls into question the very foundation of our century-old system of drug regulation." *Id.* at 1.

27 Slip op. at 26, 51.

Legal Significance

The impact that the *Caronia* decision will have on off-label prosecutions and False Claims Act litigation remains to be seen. To be sure, the Second Circuit assumed that the government could still use a manufacturer's off-label speech as evidence of an intent to distribute a drug without adequate directions for use. But in two footnotes, the court of appeals cast significant doubt on the viability of even this narrower approach.[28] As the court noted, it "remains unclear how the government would identify criminal misbranding from communications between drug manufacturers and physicians authorized to prescribe drugs for off-label use."[29] However, the court recognized that false or misleading speech is not protected under the First Amendment, and could therefore form the basis for a misbranding charge.

While the decision is subject to potential rehearing en banc or even a certiorari petition, the decision may, over time, precipitate changes in FDA's regulatory approach, including rewriting current regulations and guidance to reflect a much more narrowly tailored regime for dissemination of reprints, responding to unsolicited requests for off-label information, and scientific exchange more generally. That evolution will take time. In the interim, while *Caronia* provides the healthcare industry with an important tool for responding to enforcement challenges and negotiating global settlements with the government, pharmaceutical and medical device companies still should proceed cautiously and incrementally in their day-to-day risk calibration relating to product communications.

Arnold & Porter attorneys Lisa Blatt, Jeff Handwerker and Rob Katerberg represented respondent PhRMA before the Supreme Court in Sorrell v. IMS Health Inc. Partners Rob Weiner and Jeff Handwerker represented PhRMA in both the district court proceedings and at the United States Court of Appeals for the Second Circuit. John Nassikas, who is the head of the firm's white collar practice, and Daniel Kracov, who heads the firm's FDA and

28 *Id.* at 32 n.10, 42 n.11.

29 *Id.* at 32 n.10.

healthcare practice, have extensive experience litigating and counseling clients on First Amendment and off-label promotion issues.

We hope you have found this Advisory useful. If you would like more information or assistance in addressing the issues raised in this Advisory, please feel free to contact:

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