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Caronia And The 'New' 1st Amendment Safe Harbor

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Law360, New York (December 14, 2012, 12:46 PM ET) -- The recent Second Circuit decision vacating Alfred Caronia's criminal misbranding conviction on free speech grounds has been hailed as a landmark First Amendment case and a victory for the pharmaceutical industry. Although lawyers and commentators have been arguing since the 1990s that off-label promotion (at least when accurate and nonmisleading) deserves some constitutional protection under the First Amendment, prior to Caronia efforts to get the issue before the federal courts have come up short.

Amendment protection, will the U.S. Food and Drug Administration someday have to consider drafting guidance on a First Amendment safe harbor?

Setting the Stage for Caronia

In the 1990s, the Washington Legal Foundation (WLF) filed several suits against the FDA's off-label restrictions in the context of industry dissemination of reprint articles and reference texts (guidances on enduring materials) and its involvement in continuing medical education programs (CME guidance).

In its first opinion, the United States District Court for the District of Columbia determined that the FDA's three guidance documents on these subjects regulated manufacturer commercial free speech and by restricting considerably more speech than necessary to advance the government's interest in encouraging manufacturers to seek FDA approval for off-label uses, failed the test set forth in Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n, 447 U.S. 557 (1980). Based on its ruling, the district court enjoined the FDA from prohibiting manufacturers from disseminating enduring materials or from suggesting content to CME providers. Washington Legal Foundation v. Friedman, 13 F.Supp.2d 51, 62-75 (D.D.C. 1998) (WLF I).

Following the injunction, the FDA Modernization Act of 1997 (FDAMA) went into effect, which included a provision relating to enduring materials at 21 U.S.C. § 360aaa(b)(1)-(6). Despite the government's subsequent attempt to confine the district court's injunction to the guidance documents, the court eventually applied its injunction to the FDA's "underlying policies" related to off-label promotion.

Then, in a subsequent opinion, the court held that the FDAMA's provisions, like the guidances on enduring materials that preceded them, violated the First Amendment. See Washington Legal Foundation v. Henney, 56 F.Supp. 81 (D.D.C. 1999) (WLF III). On appeal, the government at oral argument announced that the FDAMA's superseding enduring materials provisions and the CME guidance established nothing more than "safe harbors" ensuring that certain manufacturer actions would not be used against them in "misbranding" and "intended use" enforcement actions and that neither the FDAMA nor the CME guidance authorized the FDA to prohibit or sanction speech. Washington Legal Foundation v. Henney, 202 F.3d 331, 334 (D.C. Cir. 2000) (Henney).

By re-framing the FDA's policies before the circuit court as ones in which manufacturer compliance with the FDA's safe harbors would not be used as evidence of misbranding — but that non-compliance could be used as such evidence (and with WLF acquiescence on this point) — the government essentially took the constitutional issue off the table. Finding no constitutional controversy between the parties, the court vacated the district court's decisions and injunctions. Henney, 202 F.3d at 336-37.

Having dodged the First Amendment bullet in Henney, the government unleashed a torrent of off-label investigations aimed primarily at pharmaceutical companies. In the years between Henney and Caronia, the government secured dozens of settlements with, and collected more than $10 billion in criminal and civil penalties from, the pharmaceutical industry.

While Allergan was among the companies that settled with the government during this period in connection with its highly successful Botox product, before doing so, the company filed a suit against the FDA for declaratory and injunctive relief in federal court. The suit challenged the agency's off-label regulatory scheme as violating Allergan's First Amendment right to disseminate, and the medical community's right to receive, important information related to the off-label use of Botox.

The thrust of the suit's argument was that the FDA's enforcement of the "intended use" regulation at 21 C.F.R. § 201.128 and the "new drug" statute at 21 U.S.C. § 355, created a "Catch 22" that effectively prohibited companies from speaking with physicians and others about off-label uses even where such communications were essential for the safe and effective off-label use of its product.

According to briefs before the district court, a manufacturer that knows that its drug is being used off-label and fails to provide adequate directions for the drug's safe and effective use violates the intended use regulation; but, once the manufacturer provides adequate directions to avoid liability under the intended use regulation, it has introduced a "new drug" into interstate commerce, violating the new drug statute.

For its part, the government argued that the FDA's off-label regulations, particularly the intended use regulation, did not criminalize or prohibit off-label speech but merely used such speech as objective evidence that the manufacturer intended the drug to be used off-label.

Because the case settled, the district court never addressed the suit's First Amendment challenge and the government's response.

Caronia's Impact

Despite the government's success in evading the constitutional question in the Henney and Allergan cases, its hand was forced once it pursued a criminal conviction against an individual who, unlike a publicly traded manufacturer, had nothing to lose in pressing the First Amendment argument.

In the aftermath of last week's majority opinion in Caronia, which held that truthful, nonmisleading off-label speech is constitutionally protected, only two important questions remain. First, will the opinion stand? Second, if it does, can manufacturers actually promote off-label?

A reading of the majority and dissenting opinions in Caronia confirms that both sides are in agreement on one important point: The government has a substantial interest in ensuring the integrity of the FDA drug approval process and encouraging manufacturers to submit new indications to the FDA for approval. Their divergence is based on whether Caronia's off-label speech was at issue and, even if it was, whether the FDA's regulations are constitutional under Central Hudson.

According to the majority, its decision was based on a reading of the trial record, which showed that Caronia was convicted entirely on the basis of off-label speech. Once it concluded that Caronia's conviction rested on speech, the majority applied Central Hudson and Sorrell v. IMS Health Inc., 131 S. Ct. 2653 (2011), to vacate the conviction. Reasoning that the FDA's regulations regulated "content" (favoring on-label speech and disfavoring off-label speech) and discriminated among speaker viewpoints (penalizing manufacturers, but not physicians, academics and others), the majority held that Central Hudson's "heightened scrutiny" standard applied.

Under the heightened scrutiny standard, the majority found that while the government had substantial interests in ensuring drug safety, public health and the integrity of the the FDA drug approval process, the FDA's off-label regulations neither directly advanced those interests nor were narrowly drawn to further the interests served. The majority noted several examples of less restrictive regulations that could more effectively advance the government's interests, including "warning or disclaimer systems" that could alert physicians that certain uses were not the FDA approved.

Significantly, the majority did not reject the government's argument (or the dissent's) that speech can be used as evidence of intent. However, given that the government relied solely on Caronia's speech to convict him, the majority effectively ruled that in proving off-label intent, the government must rely on more than just a manufacturer's or its representative's truthful, off-label speech.

Conversely, the majority also noted that the First Amendment only protects accurate, truthful and nonmisleading speech — anything else merits no First Amendment protection. In fact, given that Caronia made claims that appear even now as misleading (e.g., that Xyrem was "a very safe drug" despite the presence of a black box warning), the majority could have upheld his conviction under the standard it announced.

Despite the majority's assessment of its holding, the dissent recognized the implications for the FDA off-label enforcement. Arguing that Caronia's misbranding conviction rested on more than just his off-label speech, the dissent all but conceded that the government would be unable to prove off-label intent without off-label speech: "I ... fail to see how the majority's reasoning would ever allow such speech to support a conviction under 21 U.S.C. § 331(a)."

The dissent specifically agreed with the government's argument that off-label speech, no matter how truthful, could be used to prove off-label intent and that the majority's holding was a departure from established First Amendment precedent.

Conversely, the dissent noted, by way of several (often humorous) examples, that even where the underlying activity may be legal or not prohibited, promoting the activity through speech might well be unlawful — e.g., lawful for merchants to raise prices but not agree on "fixing" them; not prohibited to consume arsenic but unlawful to advocate its consumption to and by others; etc.

None of these examples, however, are analogous to Caronia's situation, where neither the underlying conduct (off-label use) nor its promotion were prohibited, except as to manufacturers.

The dissent also argued that even if the court were required to treat Caronia's speech as more than just evidence of intent, the FDA's regulatory scheme was still constitutional under Central Hudson and Sorrell. Noting the government's substantial interest in the the FDA drug review process, the dissent argued that the the FDA's prohibition on manufacturer off-label marketing directly advanced the government's interest, since absent such a prohibition, manufacturers "would have little incentive to seek the FDA approval for [off-label] uses;" and was properly limited to manufacturers because "they are the precise group that the government must encourage to participate in the new drug approval process."

Finally, the dissent remarked that the majority's examples of less restrictive alternatives to advance the government's interests would not be as effective as prohibiting manufacturer off-label promotion, further justifying the FDA's "content and speaker-based" regulations.

The Future of a First Amendment Safe Harbor

Certainly, the Caronia decision could have gone either way, and it is far from certain what will happen should there be en banc or Supreme Court review. However, assuming that the decision stands, what practical implications are there for the industry and for the government?

In the short term, the "other case" to watch is the ongoing litigation between the government and Par Pharmaceutical over the latter's Allergan-like lawsuit, challenging the application of the FDA's intended use regulation to on-label speech in an off-label setting. Although both sides have been discussing settlement for months, Caronia should strengthen Par's hand: If truthful off-label speech is protected under the First Amendment, it follows that truthful on-label speech must also be protected. Of course, if there is a settlement, Caronia's impact on the outcome may never be known.

In the long term, and especially if endorsed en banc or by the Supreme Court in some form, the Caronia decision could and should lead to the development of guidance that would operate as a First Amendment safe harbor that goes well beyond the draft guidance on "Responding to Unsolicited Requests for Off-Label Information," which the FDA issued a year ago. As evident from the briefs filed in the Par litigation, there are a number of established medically accepted off-label uses listed in approved medical compendia, the costs of which are often reimbursed by Medicare, Medicaid and other federal healthcare programs.

Although the concept of a FDA guidance document that a manufacturer's "promotional materials review committee" could use in reviewing both on and off-label materials for accuracy, truthfulness and fair balance may seem far off, it is no longer beyond the realm of possibility.

--By Jose P. Sierra

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