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Caronia And Harkonen — Lessons For The Gov't

Law360, New York (April 23, 2013, 1:15 PM ET) -- While a slight modification of the ancient biblical pronouncement, this is the core message of the Second Circuit's opinion in United States v. Caronia[1] opinion, when viewed in light of the Ninth Circuit's ruling in United States v. Harkonen.[2]

When the Second Circuit issued its opinion in Caronia this past December, it was the first time that the government had faced appellate review of its off-label prosecution theories predicated on a record of truth. It didn't matter — the government urged the Second Circuit that everything Caronia asserted was truthful.

What mattered was that he was urging his customers to use a product outside the boundaries of the permission slip that his company had obtained from the U.S. Food and Drug Administration. As the government argued in his trial, "[h]e knew the rules: you can't promote and market Xyrem for uses that have not been approved by the FDA."[3]

The Second Circuit rejected this theory, declining "the government's invitation to construe the [Food, Drug and Cosmetic Act's] misbranding provisions to criminalize the simple promotion of a drug's off-label use by pharmaceutical manufacturers and their representatives."[4]

In the immediate aftermath of the Caronia decision, opinions abounded on its impact on the government's off-label promotion prosecution campaign. Some writers urged that the government needed to rethink the entire campaign; others predicted that the decision would eviscerate federal law enforcement in this arena, and still others predicted that the government would not easily abandon an arena in which it has been quite successful in reaping huge monetary settlements.[5]

With the Harkonen decision, the debate has continued, with thoughtful legal scholars predicting both more and fewer off-label promotion prosecutions.[6]

Assuredly afraid that the U.S. Supreme Court might affirm the Second Circuit, the U.S. Department of Justice and the FDA determined to not appeal the decision. In what can be fairly characterized as a public relations campaign following that nonappeal decision, Deputy Assistant Attorney General Maame Ewusi-Mensah Frimpong told an industry conference in January, "[t]echnically speaking, in how we actually try the cases, it's not the speech itself which is illegal," she said, "[i]t's misbranding the drug and the intended use."[7]

At the same conference, Tom Abrams, director of the FDA's Office of Prescription Drug Promotion, rejected the view that the Caronia decision significantly altered the legal landscape.

Because the court did not address the constitutionality of a prosecution resting on that theory, and because the court also acknowledged that the First Amendment did not preclude an enforcement action based on speech regarding unapproved uses that was false or misleading, the Second Circuit’s decision does not bar the government from

continuing to enforce the misbranding provisions of the FD&C Act, including through criminal prosecution where appropriate, in cases involving off-label promotion.

More generally, the decision does not strike down any provision of the FD&C Act or its implementing regulations or find a conflict between the act's misbranding provisions and the First Amendment or call into question the validity of the act's drug approval framework.[8]

So, where do things stand? Is Frimpong correct that the cases are not about the speech being illegal but rather the conduct engaged in by the individual? Is it and should it be "business as usual" for the government's enforcement campaign? Because of the relative dearth of appeals in this arena, commentators on both sides are wont to make broad pronouncements from single case events.

In reality, whether a particular prosecution is wise, and how best to defend it, will depend on the specific facts of the case and the battleground — i.e., the charges — the particular prosecution team chose for itself.

The government and industry can learn from a careful comparison and analysis of the prosecutions of W. Scott Harkonen and the Ninth Circuit decision affirming his conviction for wire fraud juxtaposed against the prosecution of Alfred Caronia and the Second Circuit's reversal of his conviction for misdemeanor misbranding through off-label promotion.

To understand what the juries did in each case, and to put in context the court of appeals rulings, it is critical to compare the material facts of each prosecution side by side.

The defendant's position:

- Caronia: specialty sales consultant with a territory in New York
- Harkonen: CEO

The drug:

- Caronia: Xyrem, a "powerful central nervous system depressant" with "serious side effects" including "dependence, severe withdrawal, coma, and death"[9], which was approved by the FDA for two indications involving patients suffering from narcolepsy, with a black box warning reflecting that "safety and efficacy were not established in patients under 16 years of age."[10]
- Harkonen: Actimmune, approved in 1990 for one indication (treatment of chronic granulomatous disease) and approved in 2000 for a second indication (treatment of severe, malignant osteoporosis), which was not approved for treatment of idiopathic pulmonary fibrosis, a fatal lung disease. According to the indictment, in October 2000, Intermune commenced a phase III clinical trial "to determine whether treating IPF patients … with Actimmune. In August 2002, data from that clinical trial failed to show that Actimmune was effective in treating IPF."[11]

Charged conduct:

- Caronia: While the initial indictment charged off-label promotion as a felony and asserted that Caronia had made false statements in promoting the drug off-label, the government subsequently superseded the indictment with an information charging only misdemeanor misbranding. Core evidence included recorded

conversations between Caronia and a physician reflecting off-label promotion.[12] In one conversation, Caronia also stated, "patients as young as 14 [are] using it" and that Xyrem is a "very safe drug."[13] The drug was not approved for use in juveniles.

- Harkonen: Indictment charged Harkonen with wire fraud and with misbranding with intent to defraud or mislead. According to the indictment, Harkonen and others began to promote Actimmune to treat IPF in October 2000, simultaneously with the commencement of the clinical trial. In August, 2002, Harkonen directed that the company issue a press release with the headline: "Intermune Announces Phase III Data Demonstrating Survival Benefit of Actimmune in IPF" and a subheading reading: "Reduces Mortality by 70% in Patients with Mild to Moderate Disease."[14]

Alleged motive:

- Caronia: None stated in the opinion; it can be inferred that Caronia, as a sales representative, received a bonus based on sales.
- Harkonen: Ninth Circuit noted Harkonen's "clear financial incentive to find a positive result in the face of [the trial's] failure to meet its pre-determined goals" as supportive of jury's determination that he had "the specific intent to defraud."[15]

The criminal charges:

- Caronia:
  - Count 1: conspiracy to introduce a misbranded drug into interstate commerce in violation of 21 U.S.C. §§ 331(a) and 333(a)(1).
  - Count 2: introducing a misbranded drug into interstate commerce, in violation of 21 U.S.C. §§ 331(a) and 331(k).[16]
  - Government is not required to prove any criminal intent for either count.
- Harkonen:
  - Count 1: felony wire fraud charges, 18 U.S.C. § 1343. Government required to prove "scheme or artifice to defraud, or for obtaining money … by means of false or fraudulent pretenses, representations or promises."[17]
  - Count 2: distributing a misbranded drug into interstate commerce with "intent to defraud or mislead" and making false and misleading statements in furtherance of that distribution in violation of 21 U.S.C. §§ 331(k) and 333(a)(2).

Evidence at trial of misleading statements:

- Caronia: none.
- Harkonen: in addition to the statements noted elsewhere, evidence included: a statement that Harkonen "did not want the FDA to know about all his post-hoc analyses … 'didn't want to make it look like we were doing repeated analyses looking for a better result;'" a statement that he would "'cut that data and slice it until [he] got the kind of results [he was] looking for'" and an admission that he "was "'very apologetic'" about the Press Release's misleading nature."[18]

Evidence at trial of impact of criminal conduct (proof of harm):

- Caronia: none noted by the Second Circuit. The Second Circuit, however, made this observation: "As 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."[19]

- Harkonen: "[T]here is sufficient evidence that the Press Release was at least 'capable' of influencing the decision of doctors to prescribe, or patients to seek, prescriptions of Actimmune … because the Press Release was purportedly a very effective marketing tool."[20]

Jury outcome:

- Caronia:
  - Count 1: Jury convicted Caronia of conspiring to introduce a misbranded drug into interstate commerce (while also concluding that he had not conspired to do acts, after the drug had been distributed, that caused the drug to be misbranded).

  - Count 2: Jury acquitted Caronia of distributing a misbranded drug into interstate commerce.[21]

- Harkonen:
  - Count 1: Jury convicted Harkonen of wire fraud for "putting out [a] fraudulent press release."

  - Count 2: Jury acquitted Harkonen of distribution of a misbranded drug with intent to defraud or mislead.[22]

Court of Appeals statements on defendant's speech:

- Caronia:
  - "[G]overnment repeatedly argued that Caronia engaged in criminal conduct by promoting and marketing the off-label use of Xyrem ... The government never suggested, for example, that Caronia conspired to place false or deficient labeling on a drug."[23]

  - "[T]he proscribed conduct for which Caronia was prosecuted was precisely his speech in aid of pharmaceutical marketing."[24]

  - "While some off-label information could certainly be misleading or unhelpful, this case does not involve false or misleading promotion."[25]

- Harkonen:
  - "[T]he core constitutional issue in Harkonen's case is whether the facts the jury found establish that the Press Release was fraudulent."[26]

  - "At trial, nearly everybody actually involved in the GIPF-001 clinical trial testified that the Press Release misrepresented GIPF-001's results."[27]

  - "Because they are supported by sufficient evidence, we defer to the jury's findings that the Press Release was misleading, that Harkonen knew it was misleading, and that Harkonen had the specific intent to defraud."[28]

To date, the government has lost the only two off-label promotion prosecution charges

it has brought against drug company employees.[29] In Harkonen, where it had evidence of misleading statements by the chief executive officer, the government charged the off-label promotion as a felony, done with intent to defraud or mislead.[30]

In Caronia, where the case did not involve "false or misleading promotion," the government charged a sales representative with the off-label promotion as a misdemeanor.[31] While in both cases, the government ultimately lost, it is significant that in Harkonen, where the jury plainly concluded that for purposes of its decision to convict Harkonen of wire fraud, the defendant had, as a part of a scheme or artifice to defraud, issued or caused the issuance of a misleading press release, which exaggerated the efficacy of the drug. The jury determined to acquit Harkonen of the charge of misbranding with intent to defraud or mislead.

There can be little question that the landscape has shifted. Securing a final conviction in a misbranding case, based not upon a false or misleading label on the drug but rather upon oral statements made in promoting the drug for a nonapproved use, is, at best, a difficult quagmire for the government.

Where the statements by a putative defendant are truthful and not false or misleading, the government should expect in every case that the defendant will be acquitted, if not by the jury, then by the court of appeals. The lack of curb — jury — appeal in such a case will be readily apparent, and the government will be in the impossible position of trying to convince the jury and the court that truthful statements made to promote a drug for an unapproved use are worthy of criminal punishment.

While legal hairs can be split — and indeed have been by prosecutors, regulatory lawyers and defense counsel over the legal efficacy of off-label promotion prosecutions since the issuance of the Caronia opinion — juries will not split those same hairs. All counsel should expect that federal judges will, in future off-label promotion prosecutions in every circuit, necessarily provide to juries a Caronia-style instruction on the government's limits in prosecuting speech.

Where the jury finds the speech that is entwined in the charged conduct to be truthful and not misleading, the defendant will be acquitted. Certainly, in every case, defense counsel will seek such an instruction, and prosecutors will be hard pressed to muster convincing arguments as to why the court should not make such an instruction.

Even, however, in the face of misleading speech, proving the case to the jury's satisfaction — that the drug was misbranded and that the defendant acted with intent to defraud or mislead in distributing that misbranded product — is not a slam dunk.

Such evidence was present in the Harkonen case: He was a CEO, the jury found he had participated in a scheme to defraud physicians and patients, yet the jury still acquitted him of the off-label promotion charge. Criminal trials tend to focus on the evil that the defendant allegedly engaged in and whether the defendant's conduct was bad and whether the defendant therefore should be punished.

Lawyers on both sides of the case should do the same from the outset of the investigation. The conundrum for the government is that the actual off-label use is not illegal; rather, the prohibited conduct is the manner by which the physician came to use the product for an indication not on the label.

When a defendant does not lie in the off-label promotion, or the government fails in its ability to prove that a doctor was influenced by a defendant's lie in choosing to use the drug or device in an off-label manner, then the government should expect an acquittal. Note above the Ninth Circuit's specific reference to the power of the misleading press release to influence physicians and patients.

With that expectation in mind, the government should adjust its charging practices accordingly. Where the government cannot prove that the defendant did not lie to or

otherwise mislead the physician or her patient while engaging in off-label promotion, then the government should take a pass on any prosecution.

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[1] 703 F.3d 149 (2d Cir. 2012).

[2] Nos. 11-10209, 11-10242 (9th Cir. Mar. 4, 2013).

[3] Caronia, 703 F.3d at 158.

[4] Id. at 162.

[5] See, e.g., http://www.gibsondunn.com/publications/pages/SecondCircuit-Holds-CriminalConviction-OffLabelPromotion-ViolatesFirstAmendment.aspx ("The End of Off-Label Prosecutions? The Second Circuit Rules That a Pharmaceutical Sales Representative's Criminal Conviction for Off-Label Promotion Violates the First Amendment"); http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2012/12/a-deep-dive-into-the-second-circuits-caronia-decision-potential-next-steps-and-potential-enforcement.html ("The Second Circuit's holding represents an unmistakable setback for the government from continuing business as usual."); http://www.jdsupra.com/legalnews/second-circuit-holds-that-criminal-penal-60231/ ("The Second Circuit's opinion is poised to significantly change the landscape for companies and individuals involved in the promotion of pharmaceuticals and medical devices. If upheld through the appellate process, the decision will have a profound impact on current government investigations and prosecutions for off-label promotion, and may lead to significant revisions in corporate compliance programs.").

[6] See, e.g., Ninth Circuit Off-Label Marketing Decision Suggests More Prosecutions Will Be Coming, by David L. Douglass, http://www.natlawreview.com/article/ninth-circuit-label-marketing-decision-suggests-more-prosecutions-will-be-coming; Ninth Circuit Affirms Conviction in Harkonen, Rejects the Defendant's "Off-Label" First Amendment Challenge, by Thomas Lee and Vernon Francis, http://www.jdsupra.com/legalnews/ninth-circuit-affirms-conviction-in-hark-69966/.

[7] http://www.law360.com/articles/411149/drug-misbranding-investigations-remain-top-priority-doj.

[8] http://blog.pharmexec.com/2013/01/30/tom-abrams-caronia-won%E2%80%99t-stop-off-label-enforcement/.

[9] Caronia, 703 F.3d at 155.

[10] Id. at 155.

[11] United States v. Harkonen, Nos. 11-10209, 11-10242, 2013 WL 782354, at *3 (9th Cir. March 4, 2013).

[12] Caronia, at 156 (internal citations omitted).

[13] Id. at 156-57 (internal citations omitted).

[14] Indictment at 9, United States v. Harkonen, No. 08-00164 (N.D. Cal. March 18, 2008).

[15] Harkonen, 2013 WL 782354, at *2.

[16] Superseding Misdemeanor Information at 3-4, United States v. Caronia, No. 06-00229 (E.D.N.Y. Aug. 19, 2008).

[17] 18 U.S.C. § 1343.

[18] Harkonen, 2013 WL 782354, at *1-2 (internal citations omitted).

[19] Caronia, 703 F.3d at 166.

[20] Harkonen, 2013 WL 782354, at *2.

[21] Verdict Sheet at 1-2, United States v. Caronia, No. 06-00229 (E.D.N.Y. October 23, 2008).

[22] United States' Sentencing Memorandum at 7, United States v. Harkonen, No. 08-00164 (N.D. Cal. October 27, 2010).

[23] Id. at 161.

[24] Id. at 162.

[25] Id. at 167.

[26] Harkonen, 11-10242, at *1.

[27] Id.

[28] Id. at *2.

[29] While some commentators have referred to the prosecution in United States v. Caputo, 517 F.3d 935 (7th Cir. 2008) as an off-label prosecution, we believe that it is not. As that court noted, "defendants Caputo and Riley effectively carried out a bait-and-switch scheme on the FDA and its customers, obtaining clearance on one sterilizer but using the clearance to sell another." Id. at 978.

[30] Indictment at 1, United States v. Harkonen, No. 08-00164 (N.D. Cal. March 18, 2008).

[31] Caronia, 703 F.3d at 167.