DRUG AND DEVICE BULLETIN

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FEDERAL COURT ENJOINS ENFORCEMENT OF TRUTHFUL "OFF-LABEL" MARKETING

A federal court in New York has granted a motion for a preliminary injunction in favor of Amarin Pharma Inc., barring the U.S. Food and Drug Administration (FDA) from blocking certain truthful and nonmisleading statements by Amarin about off-label uses of its omega-3 drug, Vascepa®. *Amarin Pharma v. U.S. Food and Drug Administration*, No. 1:15-cv-03588 (S.D.N.Y., order entered August 7, 2015).

The decision comes in the wake of the Second Circuit's landmark ruling in *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012), in which the court overturned the conviction of a pharmaceutical sales representative who had promoted the off-label use of a drug using only truthful and non-misleading speech. In *Caronia,* the court of appeals ruled that, to avoid infringing First Amendment protections, "the government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA [Federal Food, Drug, and Cosmetic Act] for speech promoting the lawful, off-label use of an FDA-approved drug." To do so would impermissibly criminalize protected speech and violate First Amendment rights, the court held. FDA viewed the decision as a narrow one and indicated that it would continue its aggressive enforcement against off-label pharmaceutical drug promotion. And indeed it did, forcing settlements within months of the *Caronia* decision in misbranding/off-label actions against Amgen for $762 million and Par Pharmaceutical for $45 million.

Vascepa® Background

In July 2012, FDA approved the use of Vascepa to treat adult patients with very high triglyceride levels (above 500mg/dL). Amarin later sought approval to market the drug for patients with persistently high triglyceride levels between 200 and 499 mg/dL. An FDA-approved study confirmed that the drug is effective in reducing such triglyceride levels, yet the FDA nonetheless rejected Amarin's application for expanded approval because it was not clear that reduction of triglyceride levels alone would significantly reduce the risk for cardiovascular events in

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For more information about our Government and Regulatory Practice, please contact:

David Maria
202.783.8400
dmaria@shb.com

For more information about our Pharmaceutical and Medical Device Practice, please contact:

Madeleine McDonough
816.474.6550
202.783.8400
mmcdonough@shb.com

patients with persistently high triglyceride levels. FDA refused to authorize marketing of the drug for these patients until Amarin could show that the drug indeed reduced overall cardiovascular risk in patients. Nor was Amarin permitted to include the study results in the Vascepa label. In its letter to Amarin rejecting expanded use of Vascepa, FDA indicated that it would bring legal action if the company promoted the drug for use outside its approved bounds.

Instant Decision

In May 2015, Amarin and a group of doctors filed a complaint against FDA seeking to lift the threat of legal action by raising a First Amendment challenge to the FDCA regulations that prohibited Amarin from disseminating truthful and non-misleading statements about Vascepa to health care professionals. Specifically, they argued that, according to the precedent set forth in *Caronia*, FDA does not have the authority to bring a misbranding action against a manufacturer based solely on truthful and non-misleading statements promoting an off-label use. FDA responded that it believed *Caronia* to be a fact-bound decision that hinged on the particular jury instructions and the government's closing argument but did not broadly preclude misbranding actions, even if off-label promotion efforts consisted of truthful and non-misleading speech.

In a 69-page decision, U.S. District Judge Paul Engelmayer rejected FDA's limited interpretation of *Caronia*, holding broadly "that the FDCA's misbranding provisions cannot constitutionally criminalize, and therefore do not reach, the act of truthful and non-misleading speech promoting off-label use." Therefore, the FDCA, "categorically, [does] not reach a manufacturer or its representative under those circumstances." The court, however, cautioned that the First Amendment could not shield manufacturers or their representatives from false or misleading speech and that its protections were limited to expression, not conduct. And, while curtailing FDA's ability to bring particular misbranding actions, it counseled that it would still be wise for manufacturers to consult with FDA before promoting off-label use, as it can be a fine line between misleading and non-misleading speech.

ABOUT SHOOK

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Leading pharmaceutical and medical device companies rely on Shook to advance their business interests in the courtroom and beyond. More than 100 Shook attorneys are involved in the defense of product liability, commercial, intellectual property, and other litigation specifically for pharmaceutical and medical device manufacturers. We also help them prepare for state and federal regulatory changes, respond to government charges and investigations, or engage in strategic influence initiatives to improve the political climate in which they operate.

Our lawyers handle various enforcement and rulemaking proceedings in addition to advising on risk and compliance matters in connection with the manufacture, sale and promotion of products; clinical trials; approval pathways; labeling; safety; facility and product registration; facility inspections; custom holds; and product withdrawals and recalls. We also work with clients to establish and maintain effective corporate compliance programs, including legal risk assessments, internal investigations and record-keeping audits.

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Future of Off-Label Promotion Enforcement

What is clear in the wake of the *Amarin* decision is perhaps little. Judge Engelmayer's decision establishes that FDA cannot successfully bring misbranding actions against drug manufacturers or their representatives for truthful and non-misleading off-label drug promotion in the Southern District of New York, but it is unclear whether this analysis will gain traction outside Second Circuit courts. Even if this reasoning is adopted in other circuits, FDA will still retain the ability to bring off-label enforcement actions when the marketing is misleading or not demonstrably supported by scientific data. The focus will likely shift from asking *if* off-label uses were discussed with medical professionals to an inquiry about the specific language used in speaking with medical professionals. Accordingly, any company deciding proactively to market non-approved uses of a drug must take great care in determining the specific statements and marketing materials to be used and ensure that its representatives follow the vetted script. FDA has indicated that it would soon issue new guidelines for off-label promotion but no timetable has yet been established. At a minimum, *Amarin* and *Caronia* will certainly change the manner in which individuals and companies may defend themselves if they are the subject of an investigation for off-label marketing.