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Amarin v. FDA—Can the Current FDA Drug Approval Regime Survive?

BY BERT W. REIN

In *Amarin Pharma, Inc. v. United States Food and Drug Administration*, Amarin launched what the FDA termed ''a frontal assault . . . on the framework for new drug approval that Congress created in 1962.'' On August 7, Judge Paul Engelmayer of the U.S. District Court for the Southern District of New York responded with the ''short answer'' that the framework itself ''predates modern First Amendment law respecting commercial speech'' requiring that the 1962 Act ''must be considered, and to the extent ambiguous construed, in light of contemporary First Amendment law'' (13 PLIR 1159, 8/14/15). The Court then emphatically and unambiguously declared, following the Second Circuit's earlier ruling in *United States v. Caronia*, that Amarin was constitutionally entitled to ''engage in truthful and non-misleading speech promoting the off-label use of [its drug] Vascepa . . . and . . . such speech may not form the basis of a prosecution for misbranding.''

Faced with a decision which it believes ''has the potential to eviscerate [the] FDA drug approval regime,'' FDA has the option to appeal to a hostile Second Circuit – the progenitor of the fundamental decision in *Caronia* – with the hope of eventual Supreme Court review or, as it did in *Caronia*, accept the decision and attempt to limit its reach and effect. If FDA chooses to fight another day, it either may seek to vindicate its speech restriction policies in another Circuit or to pursue two off-label enforcement opportunities that lie open under the District Court's decision.

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First, the FDA may seek to fly-speck off-label disseminations by pharmaceutical manufacturers and argue that they are actually, rather than potentially, false or misleading and thus outside the constitutional protection accorded commercial speech. *Second*, FDA might try to identify drug company conduct going beyond merely providing information that could be the trigger for an unauthorized off-label marketing allegation using protected speech only as evidence of the manufacturer's intent to stimulate off-label use, an avenue expressly left open by the *Amarin* decision.

While FDA might create some *in terrorem* restraint on manufacturers by signaling that it will resort to one or both of these tactics, it might also conclude that *Amarin* opens the off-label flood gates which can only be shut by reversal on appeal.

One additional factor that could influence FDA's decision on appealing is the potential impact of *Amarin* on the Government's heretofore lucrative pursuit of off-label based False Claims Act (FCA) actions. Judge Engelmayer recognized the Government's position that off-label promotion could induce off-label prescribing for government-insured patients which, while not legally reimbursable, is essentially undetectable at the time a prescription is presented. However, the Court concluded that Amarin's request for protection against such an FCA inducement challenge was not ripe in the absence of an immediate enforcement threat and declined to address the First Amendment's impact on such a proceeding.

Pharmaceutical manufacturers targeted under the FCA because of off-label promotion now can raise the *Amarin* contention that such an action unconstitutionally burdens their First Amendment rights at the thresh-

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old without foregoing the option, if unsuccessful, to later settle and avoid the collateral consequences of an adverse FCA merits determination. The Government could respond that the action giving rise to the FCA claim was off-label prescribing and the consequent presentation of undisclosed off-label prescriptions for unauthorized Medicare/Medicaid co-pay coverages, invoking off-label speech legitimately to prove the manufacturer's intent to cause off-label prescribing that foreseeably generated false claims. As Amarin's unrequited request for relief suggests, the issue is not free from doubt and the consequences—witness past multibillion dollar levies—are massive for both sides. Because *Amarin* can be appealed exclusively on FDCA grounds, the Government may conclude that an appeal could bolster its FCA position while not putting its theory of inducement-based FCA violations at direct risk.

Whether FDA seeks appellate review in *Amarin* or waits to bring a subsequent challenge to off-label promotion in another Circuit, FDA's concern about the viability of the drug approval system is quite realistic. FDA reads the FDCA to limit approval of a new drug or device to the indications claimed in its proposed labeling. Promotion of any other use of the drug, in FDA's view, would make it a ''new drug'' subject to a prior approval requirement to be secured by a supplemental New Drug Application (sNDA). But obtaining sNDA approval is time consuming and expensive for manufacturers and, particularly where the potential market for a new indication is limited, manufacturers will be sorely tempted to seek shelter under *Amarin* while disseminating off-label information that would otherwise underlie an sNDA. Thus, unless FDA can reverse *Amarin* and *Caronia*, not to mention the District Court for the District of Columbia's decision in *WLF v. Henney* which also recognized First Amendment protection for off-label speech, it is reasonable to expect that manufacturers will increasingly push the boundaries of discussion of off-label uses already taking place in medical journals, text books and among physicians, all of which is outside FDA's jurisdiction and, as non-commercial scientific speech, entitled to robust First Amendment protection.

Rather than trying to shore up the crumbling dam restricting manufacturer participation in the flow of off-label information, FDA (and patients) might be better served if the Agency focused instead on how best to capture and evaluate that flow to benefit the public health. The *Amarin* court observed that the fundamental problem in the FDA's off-label speech approach was that its 1962 premise—speech is simply a form of regulatable conduct—has been superseded by later changes in First Amendment commercial speech doctrine. That observation applies equally to the scientific premise that rigorous pre-approval testing provides substantially all the useful information prescribers need. Trial lawyers have long and loudly contended on behalf of injured patients that this premise is deficient on the risk side. As the court's discussion of the breadth of off-label usage demonstrates, this premise is certainly deficient on the benefit side. FDA would be well advised to abandon this fiction and establish an orderly system: to capture the ''big data'' arising from post-approval use; to ensure continuing unbiased analysis of that data; to facilitate the dissemination of truthful and non-misleading off-label information; and to respond promptly and appropriately as new risks and benefits are identified from clinical experience. Faced with what FDA itself termed ''evisceration'' of the current regulatory regime, it is high time that FDA begins to actively consider alternatives.

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