Par vs. USA – Off-label Promotion and the First Amendment

Playing the Back 9 - FDA may need to take a Mulligan (or two) in its definition of off-label promotion

By Michael A. Walsh
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More than ten years after the District Court in DC invalidated FDA regulations concerning promotional activities as violative of the First Amendment to the US Constitution in *Washington Legal Foundation v. Henney*, and as the judge who presided over that case predicted, the First Amendment challenge to FDA regulations prohibiting truthful and non-misleading speech has resurfaced.

In *Par Pharmaceutical, Inc. et al v US*, Par brought suit for declaratory relief in the District of Columbia to prohibit FDA from, among other things, enforcing "FDA's unconstitutional and invalid regulations" restricting truthful non-misleading speech. Par's complaint seeks declaratory and injunctive relief concerning the following:

1. FDA's intended use regulations "as applied" violate the first Amendment by prohibiting truthful non-misleading "on-label" speech.
2. FDA cannot "deem intent" to market off-label based on knowledge that a manufacturer knows that physicians are using a product off-label.
3. To the extent on-label speech is "deemed" to relate to an off-label use, declare that FDA's regulations violate the First Amendment to the extent they prohibit truthful and non-misleading speech concerning off-label use.
4. To the extent on-label speech is "deemed" to relate to an off-label use, declare FDA's definition of labeling violates the First Amendment "as applied" to prohibit truthful non-misleading speech concerning off-=label use.
5. 32 CFR 201.100(c)(1) is invalid as contrary to 21 USC §353(b)(2).
6. FDA's definition of labeling 21 CFR § 201.1(1)(2) is invalid as contrary to 21 USC § 321(m).
7. Enter a preliminary injunction during the pendency of this case prohibiting enforcement of the foregoing regulations.
8. Enter a permanent injunction to prevent enforcement of invalid regulations to prohibit truthful and non-misleading speech.
9. Request for costs and attorneys' fees.

In seeking to dismiss this case, FDA argued that the claims are not ripe and submitted the declaration of the Associate Director of Medical Policy and Director of the Office of Medical Policy (OMP) at the Center for Drug Evaluation and Research (CDER) at FDA. At this juncture in the case, FDA is not yet tackling Par's First Amendment challenge but is attacking what it perceives as false assumptions and misinterpretations of the

marketing regulations. FDA's Declaration starts off recognizing that an off-label use may constitute the medical standard of care and that manufacturers possess superior information concerning their products stating:

> "FDA recognizes that some off-label uses or treatment regimens may be important therapeutic options and may even constitute a medically recognized standard of care. FDA further recognizes that scientific or medical departments within drug firms often maintain a large body of information about their products, which may include off-label information for their products. FDA acknowledges that off-label information may be of use to physicians seeking information about a medical product for their patients. (Declaration at para 12).

There is no law, regulation or guidance that details the contours of permissible conduct with respect to truthful and non-misleading communications concerning off label use of an FDA approved drug or device and, in its Declaration, FDA purports to "describe... FDA's procedures and policies with respect to the communication of promotional information about off-label uses." To the extent FDA's procedures and policies are stated, they are stated like a riddle, not stating specifically what is permitted, instead stating what it is not permissible and injecting the following confounding phrase: "*by itself*." With that background, FDA explains its policies and procedures as follows:

> FDA does not consider a manufacturer's truthful and non-misleading speech to healthcare professionals concerning the approved use of an FDA-approved drug as establishing, *by itself*, a manufacturer's objective intent that the drug be used for an unapproved use. (para 14)
>
> Nor does FDA regard a manufacturer's knowledge that an FDA-approved drug was being prescribed by healthcare professionals for an unapproved use as establishing, *by itself*, a manufacturer's objective intent that the drug be used for an unapproved use.

Thus, wrongful and illegal conduct can be proven, in part, by truthful and non misleading speech and knowledge that a product is being used by the medical profession for an unapproved use. This evidence is not *per se*, "*by itself*," sufficient evidence of criminal conduct, but it is evidence nonetheless of illegal intent; such as having explosive material would not, *by itself*, be evidence of intent to cause an explosion, but also possessing the triggering materials might be evidence of illegal intent. The phrase "*by itself*" is not defined under the Act, in the regulations or in Guidance documents and is understood to have its ordinary meaning (i.e. *per se*, or unconnected to other matters). Yet, the examples FDA provides would not exist in a vacuum, unconnected to other "circumstances," events or facts (i.e. "by itself") and it remains unclear what will render conduct and surrounding circumstances actionable.

FDA sheds dim light on what evidence will suffice to render "truthful speech" or knowledge of facts illegal stating: "determining ...the manufacturer's 'objective intent,'... can be based on ...the circumstances surrounding the drug's distribution... and may include "additional evidence suggesting...a deliberate strategy to encourage off-label prescribing." (Declaration at 13 and 15). Despite purporting to provide detail, none is given and it remains unclear what constitutes "additional evidence" and whether additional "*by itself*" (i.e. truthful speech or knowledge of additional facts) conduct will expose a manufacturer to civil and criminal liability.

There is no doubt of FDA's zeal in protecting the public from products that are either unsafe or not efficacious, but in light of the articulation of the "policies and procedures" set forth by FDA in this case as well as its intransigence on this issue, the First Amendment issues raised in *Par*, and a growing number of other cases, may not be resolved any time soon. In the meantime, as discovery proceedings get underway in Par, uncertainty continues concerning the dissemination of truthful and non-misleading information regarding unapproved uses for FDA regulated products.