Risky Conduct with Risk Mitigation Strategies? The Potential Antitrust Issues Associated with REMS

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Introduction

From an antitrust perspective, the pharmaceutical sector continues to be one of the most heavily scrutinized industries in recent years. Even after a year in which the FTC reported that it had sought relief in over 97% of horizontal pharmaceutical mergers in which the agency had issued a second request since 1996,[2] and the debate over so-called pay-for-delay agreements reached another level with the Third Circuit's ruling in *K-Dur*[3] and the Supreme Court's decision to grant certiorari in *FTC v. Watson Pharmaceuticals, Inc.*,[4] new fronts of enforcement continue to emerge.

One of the latest fronts to surface in the struggle between branded and generic drug manufacturers is occurring in the context of drugs operating under a Risk Evaluation and Mitigation Strategy ("REMS"). A REMS program is a set of measures the FDA may require as a condition of approval of a drug that is believed to pose health and safety risks to certain patients taking the drug. Among the measures that might be required as part of a REMS program are medication guides and communication plans to convey the risks to patients, as well as multi-level restrictions on distribution of the drug. Increasingly generic drug manufacturers are accusing branded firms of using REMS-related distribution restrictions as a tool to prevent would-be generic competitors from entering the market. Former FTC Chairman Jon Leibowitz echoed these concerns, describing this type of conduct as "particularly troubling."[5]

Indeed, antitrust allegations related to REMS have already given rise to both a government investigation and private litigation. Most recently, however, litigation is currently pending in federal district court in New Jersey in which Actelion Pharmaceuticals, a branded manufacturer, sued generic firms— Apotex Corp. ("Apotex") and Roxane Laboratories, Inc. ("Roxane"). Actavis Elizabeth LLC ("Actavis") successfully petitioned to intervene in the case

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[2] Fed. Trade Comm'n, HORIZONTAL MERGER INVESTIGATION DATA, FISCAL YEARS 1996-2011, at 14, Table 4.5 (Jan. 2013), http://www.ftc.gov/os/2013/01/130104horizontalmergerreport.pdf.

[3] In re K-Dur Antitrust Litigation, 686 F.3d 197 (3d Cir. 2012) (holding that pharmaceutical patent settlements that restrict generic entry and involve a payment to the generic are presumptively unlawful).

[4] 677 F.3d 1298 (11th Cir. 2012).

[5] Dina El Boghdady, *Generic-drug Makers' Complaints Over Brand-Name Access Prompt Investigations*, WASH. POST, May 22, 2012, http://www.washingtonpost.com/business/economy/generic-drug-makers-complaints-over-distribution-law-provoke-investigations/2012/05/22/gIQAhExKiU_story.html.

as a counterclaim plaintiff asserting that Actelion may have an antitrust duty to supply them with samples of Actelion's drug, Tracleer, which is being marketed and distributed under a REMS (the "Tracleer litigation").

As with so many practices in the pharmaceutical sector, analyzing REMS-related issues from an antitrust perspective is a complex endeavor due to the extensive regulatory scheme in place in the industry. This article will describe the circumstances in which these issues arise, and examine the various arguments being made on both sides, specifically in the context of the ongoing Tracleer litigation.

Background

REMS were first introduced as part of the Food and Drug Administration Amendments Act of 2007 ("FDAAA"), which granted the FDA the authority to require pharmaceutical manufacturers to develop a REMS where such measures are "necessary to ensure that the benefits of the drug outweigh the risks of the drug."[6] Thus, REMS have been described as "strateg[ies] to manage…known or potential serious risk[s] associated with a drug or biological product."[7] The FDA may require a REMS for any New Drug Application ("NDA"), Abbreviated New Drug Application ("ANDA"), or Biologics License Applications ("BLA") at any stage in the product lifecycle, however the elements potentially required for a REMS may vary according to the type of application involved.[8]

The FDA can require that a REMS for a particular drug include any combination of the following elements: a medication guide and patient package insert, a communication plan, and, where necessary, "elements to assure safe use." Elements to assure safe use are essentially restrictions on the manner in which drugs are provided to patients, and are typically required where the FDA determines that a medication guide and communication guide alone will not be sufficient to mitigate the risk associated with a particular drug. Elements to assure safe use may take the form of provisions requiring that "health care providers who prescribe the drug have particular training or experience," that pharmacies that dispense the drug are specially certified, that the drug only be dispensed in certain health care settings or only to patients with evidence of safe-use conditions, or that patients using the drug be monitored or enrolled in a registry.[9] Once approved, a REMS creates enforceable obligations for the manufacturer and the FDA.[10] In many cases REMS programs are patentable.[11]

Portions of the FDAAA also address various issues that might arise when an ANDA is filed

[6] 21 U.S.C. §355-1(a)(1).

[7] U.S. FOOD AND DRUG ADMINISTRATION, *Questions and Answers on the Federal Register Notice on Drugs and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies*, http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FoodandDrugAdministrationAmendmentsActof2007/ucm095439.htm.

[8] 21 U.S.C. §355-1(i) (stating that a REMS for a drug covered under an ANDA may only be required to include a medication guide or patient package insert, and subject to exceptions, elements to assure safe use).

[9] 21 U.S.C. §355-1(f)(3).

[10] Questions and Answers, *supra* note 8 ("FDA may impose civil monetary penalties for violations of the REMS provisions or the drug or biological product can be deemed misbranded, and FDA could obtain injunctive relief.").

[11] Many branded manufacturers have sought patent protection for their REMS programs. *See e.g.*, U.S. Patent No. 7,141,018 (Celgene patent for the REMS it developed for its thalidomide product).

and the Reference Listed Drug ("RLD") is operating under a REMS, but these provisions leave many questions up in the air as to their meaning and practical effect. For example, the FDAAA anticipates that a patented REMS could effectively act as a barrier to entry for generic firms. Thus, while requiring that a generic drug and the relevant RLD generally use a "single, shared system," the FDAAA also gives the FDA the authority to waive this requirement in certain circumstances where the REMS is protected by patent or as a trade secret. Of particular controversy at the moment, however, is the question of whether a branded manufacturer can be compelled to supply a generic manufacturer with enough of the branded drug to facilitate the testing required for an ANDA. To qualify for approval under an ANDA, a generic drug must be shown to be substitutable for the branded counterpart. A generic drug product is considered to be substitutable for a branded drug if the two are "bioequivalent"—something which is typically established through testing involving samples of the branded drug. In the absence of a restrictive distribution system, including those imposed as part of a REMS, generic firms can typically acquire the samples necessary for this testing from distributors or wholesalers. However, where a REMS includes provisions barring distributors and wholesalers from selling the drug to entities without approval under the REMS, generic firms may turn to the branded manufacturers themselves to supply the drug samples directly.

Some generic firms have reported that their requests to branded firms for samples of drugs with these types of REMS programs have been denied, thereby blocking them from introducing a generic version of the drug. Branded firms, however, contend that they are under neither a statutory nor an antitrust duty to supply would-be generic competitors, particularly in circumstances that would contravene their REMS programs.[12]

Indeed, these types of allegations against one branded manufacturer have previously given rise to citizen petitions to the FDA, government investigations,[13] and private litigation. In 2008, Celgene Corp. was accused by two generic firms—Lannett Co. and Dr. Reddy's Laboratories—of using the distribution restrictions mandated under its REMS program as a pretext for refusing to provide them with samples for bioequivalence testing. Although Lannett filed suit alleging that the refusal violated §2, and Dr. Reddy's and Celgene filed dueling citizen petitions with the FDA, the litigation ultimately settled before substantive considerations of the issues, and the issues raised by in the citizen petitions were never addressed by the FDA.[14] Thus, the Tracleer

[12] *See e.g.*, Complaint for Declaratory Judgment at ¶ 36-38, Actelion Pharmaceuticals Ltd. v. Apotex Inc. and Roxane Laboratories, Inc., No. 1:12-cv-05743-NLH-AMD (D.N.J. Sept. 14, 2012); Plaintiff Actelion Pharmaceuticals Ltd.'s Memorandum of Law in Support of Plaintiffs' Motion for Judgment on the Pleadings and to Dismiss Counterclaims at 18-20, No. 1:12-cv-05743-NLH-AMD (D.N.J. Jan. 16, 2013).

[13] According to the company's SEC filings, Celgene received two Civil Investigative Demands ("CIDs") from the FTC relating to Thalomid and Revlimid—the first in the fourth quart of 2009 and a second in the fourth quarter of 2010. The filings also state that Celgene received a subpoena from the State of Connecticut which "referenced the same issues as those referenced" in the 2009 FTC CID. Form 10-Q Quarterly Report for Celgene Corp. (filed Nov. 2, 2011), http://www.sec.gov/Archives/edgar/data/816284/000110465911060043/a11-26049_110q.htm.

[14] Lannett filed suit in federal court in the Eastern District of Pennsylvania and Celgene subsequently filed a motion to dismiss the suit. Lannett Co. v. Celgene Corp., No. 08-3920 (E.D.Pa. filed Aug. 15, 2008); Defendant Celgene Corp.'s Memorandum of Law in Support of Its Renewed Motion to Dismiss, No. 08-cv-3920 (May 28, 2010). Although the court ultimately denied Celgene's motion to dismiss, it did so without issuing an opinion. *See* Order

litigation currently pending offers a fresh opportunity for further elucidation on these issues.

Actelion v. Apotex, Roxane, & Actavis

As mentioned above, in September 2012, Actelion brought suit against Apotex and Roxane[15] seeking a declaratory judgment that Actelion is under not under any duty to deal with any of the companies, nor any duty to supply them with samples of its drug, Tracleer, which is marketed and distributed under a REMS required by the FDA as a condition of approval.

A. Backgroud

Tracleer is the brand-name drug with the active ingredient bosentan, developed by Actelion for the treatment of pulmonary arterial hypertension ("PAH"). Because Tracleer can cause serious liver damage as well as birth defects, the FDA required Actelion to adopt a REMS that, among other things, includes various distribution restrictions. According to the Tracleer REMS, known as the Tracleer Access Program ("TAP"), Tracleer can "only be dispensed through pharmacies, practitioners, and in health care settings that are specially certified and bound by contract to follow a strict protocol to monitor and protect safety health."[16]

Apotex, Roxane, and Actavis all sought supplies of Tracleer in order to perform bioequivalence testing for the purpose of filing ANDAs for generic versions of the drug. According to the complaint, pursuant to the TAP, Actelion only distributes Tracleer through wholesale distributors that agree to follow the REMS.[17] As a result, the generic firms could not obtain samples on the open market and instead requested samples directly from Actelion. Actelion denied these requests, and ultimately filed suit after both Apotex and Roxane threatened to bring antitrust claims alleging that the denials were anticompetitive.[18]

Apotex and Roxane responded by filing counterclaims alleging that Actelion's refusal to supply as well as its agreements with distributors restricting supply violated §§ 1 and 2 of the Sherman Act. Although Actelion presents a variety arguments in support of its request for declaratory judgment, they are all focused on one essential question—whether Actelion, as a manufacturer of a branded drug marketed and distributed under REMS-mandated distribution restrictions, has the right to refuse to supply would-be generic competitors, or if instead it has some duty (antitrust or otherwise) to supply generic firms with the samples required for bioequivalence testing.

B. Refusal to Deal

Actelion's core contention is that except in very narrow circumstances, the antitrust laws do not impose upon firms a duty to deal or cooperate with competitors. The counterclaim-plaintiff generics companies, however, argue that the conditions created by the FDA process for approval of generic drugs together with REMS-mandated restricted distribution schemes present precisely the circumstances necessary to trigger

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Upon Consideration of Defendant Celgene Corp.'s Renewed Motion to Dismiss, No. 08-3920 (Mar. 30, 2011).

[15] As noted above, although Actelion initially filed suit against only Apotex and Roxane, Actavis successfully petitioned to intervene in the case.

[16] Complaint for Declaratory Judgment, *supra* note 12, at ¶18.

[17] *Id.* at ¶19.

[18] Indeed, Apotex went so far as to include a draft complaint with one of its letters to Actelion.

one, if not more, of the recognized exceptions to that general rule. Thus the key question at issue is whether the REMS framework and the resulting conditions in the market support the applicability of an exception.

Although the case law in this area is not always clear, and various courts have adopted a wide array of approaches and formulations, courts in the U.S. have recognized, at least in the past, two primary instances in which a unilateral refusal to deal may violate §2: (1) the unreasonable or unjustified termination of a voluntary prior course of dealing; and (2) denying a competitor access to a product or service which is an essential element for the competitor's ability to compete in a downstream market. Courts have generally narrowly interpreted both of these exceptions, however, and the ongoing validity of the latter exception is particularly questionable given the Supreme Court's recent refusal to recognize the doctrine as discussed below. The applicability of each of these exceptions to the circumstances presented by REMS is examined in greater depth below.

1. *Aspen Skiing* & the Voluntary Prior Course of Dealing Exception

The Supreme Court has recognized only a very narrow exception to the general right to unilaterally refuse to deal with a competitor, even as a monopolist—an exception that Actelion contends does not apply in the context of drugs operating under a REMS. Specifically, in *Aspen Skiing Co. v. Aspen Highlands Skiing Corp.*, the Court held that a unilateral refusal to deal with a competitor may give rise to §2 liability where it involves an unjustified cessation of a prior voluntary course of dealing between the parties.[19] The Court subsequently explained in *Trinko* that whereas the "unilateral termination of a voluntary (and thus presumably profitable) course of dealing suggest[s] a willingness to forsake short-term profits to achieve an anticompetitive end," where the defendant has not engaged in a course of dealing with rivals voluntarily "the defendant's prior conduct sheds no light upon the motivation of its refusal to deal," namely whether the alleged actions "were prompted not by competitive zeal but by anticompetitive malice."[20] While *Trinko* reaffirmed the existence of this exception, it also described *Aspen Skiing* as "at or near the outer boundary of §2 liability."[21]

It is not clear as of yet whether or to what extent the counterclaim-plaintiff generic firms in this case will press an argument based on *Aspen Skiing*, particularly in light of the fact that none of the generic firms have alleged that Actelion has supplied them with samples of Tracleer in the past.[22]

2. Drug Samples as Essential Facilities in the Presence of a REMS

Through counterclaims Apotex, Roxane, and Actavis each allege that Actelion has engaged in illegal monopolization by refusing to provide samples of Tracleer, which they argue are an essential facility for the production of generic bosentan because "[i]t is impossible for a generic manufacturer…to bring a competing bosentan product to market without access" to such samples for bioequivalence testing.[23]

[19] 472 U.S. 585 (1985).

[20] Verizon Communications Inc. v. Law Offices of Curtis V. Trinko, LLP, 540 U.S. 398, 409 (2004).

[21] *Id.*

[22] Counterclaim-plaintiffs filed their responses to Actelion's Motion for Judgment on the Pleadings and to Dismiss Counterclaims on March 4, 2013, but are not included in discussion here.

[23] Answer, Affirmative Defenses, and Counterclaim of Defendants Apotex Inc. and Apotex Corp. at ¶70. *See also* Roxane Counterclaim Complaint, *supra* note 12, at ¶142; Memorandum in Support of the Motion of Actavis

The Supreme Court has never recognized the essential facilities doctrine in the context of a unilateral refusal to deal and the doctrine is generally disfavored by courts, particularly after *Trinko*.[24] However, the few circuits that have applied the doctrine generally require that a viable essential facilities claim contain four elements:

> (1) control of the essential facility by a monopolist; (2) a competitor's inability practically or reasonably to duplicate the essential facility; (3) the denial of the use of the facility to a competitor; and (4) the feasibility of providing the facility.[25]

The generic firms argue that they can neither obtain the necessary samples from other sources, namely distributors and wholesalers, due to the REMS-mandated distribution restrictions, nor can they "practically or reasonably duplicate samples of Tracleer for the purpose of conducting a bioequivalence study that satisfies FDA's requirements" by obtaining them from other countries.[26] They also assert that it is feasible for Actelion to provide such samples at market price because Actelion is already making Tracleer available to patients in the market, and further that Actelion has failed to offer any justification for its refusal to making the drug similarly available to them.

Actelion, on the other hand, contends that courts have cast considerable doubt on the validity of the essential facilities doctrine in recent years, and to the extent it retains some validity as an antitrust theory of harm, it is inapplicable in the REMS context. First, Actelion argues that the essential facilities doctrine is intended to target situations where a monopolist leverages its control of access to an essential facility into another stage of production or market. "The doctrine arose in cases in controlled access to some infrastructure or input that was necessary to compete in a ***different*** market with a ***different*** service or product."[27] Instead, the generic firms here are seeking samples of branded bosentan (Tracleer) for the purpose of competing in the market for bosentan.

Second, Actelion asserts that the essential facilities doctrine is inapplicable where the facility at issue is a patented product. Just as U.S. courts have generally refused to recognize an antitrust offense based on a unilateral refusal to license intellectual property, patent holders are under no duty to sell patented products to competitors.

Third, and finally, Actelion disputes the notion that bioequivalence testing and the ANDA process are the only practicable means by which these firms could enter the market.[28] According to Actelion, a generic firm wishing to compete with Tracleer could either "develop drug products with the exact same formulation as

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Elizabeth LLC to Intervene as Defendant and Counterplaintiff,, at 25.

[24] *Trinko*, 540 U.S. at 411.

[25] MCI Communications v. AT&T, 708 F.2d 1081, 1132-33 (7th Cir. 1983).

[26] Apotex Counterclaim Complaint, *supra* note 23, at ¶73. Apotex was able to obtain samples of the Canadian version of Tracleer and proposed a bioequivalence study using those samples to the FDA, but the FDA rejected that proposal because FDA regulations require that this testing be done with the exact drug approved by the FDA that the ANDA-filer seeks to reference in its application. *Id*.

[27] Actelion Memorandum of Law in Support of Plaintiffs' Motion for Judgment on the Pleadings and to Dismiss Counterclaims, *supra* note 12, at 15 (emphasis original).

[28] Geneva Pharmaceuticals Tech. Corp. v. Barr Labs, Inc., 386 F.3d 485 (2d Cir. 2004) (holding that functionally interchangeable branded and generic warfarin sodium drugs were in separate markets).

Tracleer and, subject to intellectual property rights, file an NDA" or file "an application under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act" which "would allow them to make use of the FDA's previous finding of safety and efficacy."[29] The counterclaim-plaintiff generic firms, however, argue that the NDA process is both "prohibitively…slow" and "not an economically feasible path for generic entry."[30]

C. Trinko & the REMS Regulatory Framework

One of the more interesting questions at issue in this case is what, if any, impact the REMS regulatory scheme has on the antitrust analysis of refusals to deal in this context. The essence of the generic firms' allegations is that "Actelion is using REMS and distribution restrictions as a pretext to block or delay generic competition."[31] The generic firms argue that Congress explicitly contemplated and prohibited just this type of exclusionary conduct when they included in the FDAAA a provision prohibiting producers of a drug approved with a REMS from using "any element to assure safe use required by [FDA] under this subsection to block or delay approval" of an ANDA.[32]

Actelion asserts, however, that nothing in this provision, nor indeed any other part of the REMS statute, imposes additional duties or obligations on branded manufacturers to supply or cooperate with would-be generic competitors, or otherwise alters the duties required of branded firms with respect to REMS-covered drugs under the antitrust laws, assuming there are any. According to Actelion, the accuracy of this interpretation is confirmed by the fact that Congress explicitly considered and rejected language that would have imposed such a duty on multiple occasions.[33] Furthermore, even if one were to assume that this language did impose some additional duty to supply onto branded manufacturers, violation of such a provision would not create an antitrust cause of action.

Actelion relies in particular on case law from the telecommunications sector, including *Verizon Commc'ns Inc. v. Law Offices of Curtis V. Trinko, LLP*, where Congress explicitly imposed a duty to deal on incumbent firms to aid new entrants, and yet the court declined to find that violations of those statutory duties provided the basis for an antitrust claim.[34] At issue in *Trinko* were allegations that Verizon's denial of interconnection services to local exchange carrier (LEC) competitors in violation of both telecommunications statutes and related regulations, constituted unlawful monopolization under §2 of the Sherman Act.

[29] *See* 21 U.S.C. §355(b)(2); 21 C.F.R. §314.54.

[30] Proposed Counterclaims of Actavis, *supra* note 23, at ¶50, 57.

[31] Roxane Counterclaim Complaint, *supra* note 12, at ¶11.

[32] 21 U.S.C. §355-1(f)(8).

[33] In 2007, Congress considered including, but ultimately excluded from the final version of the bill, language in the FDAAA itself that would have required the holder of an application approved with a REMS to supply a firm seeking approval of an ANDA with "a sufficient amount of [the] drug to conduct bioequivalence testing" at fair market value where the REMS required by the FDA included distribution restrictions. H.R. 2900, 110th Cong. §901 (2007). In 2012, Congress again considered an amendment to the Food and Drug Administration Safety and Innovation Act that would have permitted, but not required, holders of an application approved with a REMS to supply that drug to an eligible drug developer for purposes of bioequivalence testing. S. 3187, 112th Cong. §1331 (May 24, 2012)(providing that "no elements to ensure safe use shall prohibit, or be construed or applied to prohibit, supply of such drug to any eligible drug developer for the purpose of conducting testing necessary to support [an ANDA]…").

[34] *See* Verizon Communications Inc. v. Law Offices of Curtis V. Trinko, LLP, 540 U.S. 398, 409 (2004).

While acknowledging that "[a]ntitrust analysis must always be attuned to the particular structure and circumstances of the industry at issue" and thus the regulatory context "may…be a consideration in deciding whether to recognize an expansion of the contours of §2," the Supreme Court held that such an expansion was not warranted in the circumstances presented in that case.[35] The Court distinguished this concept from the doctrine of implied immunity, explaining that in certain circumstances a regulatory scheme "significantly diminishes the likelihood of major antitrust harm,"[36] effectively making antitrust "superfluous."[37]

The Court identified several characteristics of the telecommunications regulatory scheme that counseled against expanding §2 to impose an antitrust duty to deal in that case. First, Verizon's FCC authorization to operate in the market was contingent upon its compliance with the statutory obligations to provide interconnection services.[38] Thus, violations of those commitments were subject to remediation through FCC enforcement and oversight, including the suspension or revocation of market authorization. Second, the Court emphasized that the fact that the FCC had engaged in active enforcement of the very statutory obligations at issue against Verizon demonstrated that "the regime was an effective steward of the antitrust function."[39]

The Court stated that policy considerations also disfavored any extension of §2 under the circumstances. According to the court, not only was there a risk of false positives due to the sheer number and likely technical nature of any violations of the statutory duties, but it would be very difficult for a court to effectively supervise any remedy it imposed. "Effective remediation of violations of regulatory sharing requirements will ordinarily require continuing supervision of a highly detailed decree."[40]

There are many similarities between the facts present in *Trinko* and those giving rise to REMS-related disputes. Like the telecommunications industry, the pharmaceutical sector is highly regulated. Indeed, nearly every aspect of the pharmaceutical product life cycle is defined and guided by regulation, and subject to FDA oversight. However, as evidenced by the court documents filed in the Tracleer litigation, it remains a matter of dispute whether the REMS provisions of the FDAAA actually impose a statutory duty on manufacturers of REMS-covered drugs to supply would be-ANDA filers with samples for bioequivalence testing. Even if such a duty is assumed, however, the various factors identified by the Court in *Trinko* could point in conflicting directions in terms of whether antitrust laws would have any role to play in enforcing such a duty.

If the FDAAA does impose a duty to supply, there is scant evidence that the FDA has been active in enforcing such an obligation. This may, at least in part, be due to the fact that it remains unclear whether the FDA even has any authority to enforce the prohibition against companies using a REMS to block generic entry.[41] On the other hand, the same policy

[35] *Id.* at 412.

[36] *Id.* (quoting Concord v. Boston Edison Co., 915 F.3d 17, 25 (1st Cir. 1990)).

[37] Phillip E. Areeda & Herbert Hovenkamp, ANTITRUST LAW ¶352 (2008).

[38] *Trinko*, 540 U.S. at 412-13.

[39] *Id.* at 413.

[40] *Id.* at 414-15.

[41] The FDA's primary enforcement authority is derived from the Federal Food, Drug, and Cosmetic Act (FDCA), which permits the agency to take action against "prohibited acts." 21 U.S.C. §331. Section 355-1(f)(8),

concerns weighing against antitrust intervention in *Trinko* are arguably present in the REMS context—namely the practical obstacles to effective enforcement of a duty to deal. Although unlike in *Trinko*, Actelion is already selling the drug on the market and supplying a generic for bioequivalence testing is likely to consist of a discrete number of sales over a limited period, enforcing a duty to deal would require a court to delve into whether a generic has demonstrated it is in compliance with the relevant REMS to determine whether the refusal to supply is intended to exclude or is instead merely a reasonable refusal in light of regulatory and safety concerns. Furthermore, a court may be forced to supervise whether that generic firm remains in compliance to determine whether any subsequent attempt to discontinue supply would be unreasonable.

Other Potential Issues

Even if the refusal to deal questions at the core of the Tracleer litigation are ultimately resolved, that is unlikely to remove all controversy associated with REMS. For example, resolution of the Tracleer litigation will do nothing to address questions related to access to or the sharing of the REMS program itself once generic entry is otherwise imminent. As noted previously, the FDAAA requires that a drug that is the subject of an ANDA and the associated RLD use a "single, shared [elements to assure safe use] system" where one is required.[42] The rationale for this rule is that using a common system for branded and generic versions of a particular drug is not only efficient, but also avoids conflicts that may reduce efficacy of the programs. However, the provision also contains an exception to reduce the degree to which a patented REMS system acts as a barrier to generic entry. Where the elements to assure safe use system is protected under a patent and the generic has been unable to obtain a license, the FDA will allow the ANDA-applicant to use a different, but comparable system.[43] According to the FDA website, five products currently have single shared REMS systems in place.[44]

Despite the time and expense likely involved in developing and implementing a comparable REMS system, and the potential safety concerns that might be raised by the presence of multiple systems, it seems unlikely that there is an antitrust basis upon which to challenge a branded manufacturer's decision not to license a REMS to a potential generic competitor. Still these shared REMS situations raise other questions. For example, is a brand manufacturer permitted to charge a generic firm for access to and use of its REMS?

Assuming it can, upon what basis should those payments be calculated? What types of provisions in such an agreement might raise §1 or §2 issues? In what circumstances will the FDA conclude that a license has actually been sought and denied where the brand firm offers to license the REMS at a price the generic views as excessive?

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however, does not designate the use of a REMS to block generic entry a prohibited act under the FDCA. Thus, it is unclear from where the FDA could argue that it has the authority to force a branded manufacturer to supply a generic firm with product samples for bioequivalence testing.

[42] 21 U.S.C. §355-1(i)(B).

[43] 21 U.S.C. §355-1(i)(B)(ii). The provision also contains an exception for situations where the burden of creating a shared system outweighs the benefits likely to be derived from such a system. 21 U.S.C. §355-1(i)(B)(i).

[44] U.S. Food and Drug Administration, APPROVED RISK EVALUATION AND MITIGATION STRATEGIES (REMS), http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm# (last visited Feb. 1, 2013).

Conclusion

Like the Tracleer litigation itself, it is still relatively early days in terms of the antitrust community's consideration of the implications of REMS, and so this case appears to be primed to have a significant influence in terms of the future direction of the debate. However, if the challenges of other practices in the pharmaceutical sector are any guide, regardless of the ultimate outcome of this particular litigation, REMS are likely to remain a source of questions and controversy for the foreseeable future.