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What To Watch As FDA Begins To Fight Rising Drug Prices

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With the enactment of the Hatch-Waxman Act, Congress spurred generic competitors to enter the market and lower the cost of expensive, brand-name pharmaceuticals. At the same time, to incentivize new drug development, the act provides limited regulatory exclusivity periods for drug innovators.[1] As a product's market exclusivity period wanes, drug innovators may use creative and sometimes controversial means to maintain dominance in the market and keep products free from generic competition. These anti-competitive tactics trigger the involvement of the Federal Trade Commission, but until now, the issue has not similarly stirred the U.S. Food and Drug Administration to action.

As of last month, the FDA's reluctance to engage in price-control efforts may be changing. On July 18, the FDA held a public meeting to solicit input on how it might join the fray.[2]

We now take a look at some of the controversial issues that frequently arise incident to Hatch-Waxman that the FDA may set its sights on in the near future.

Pay-for-Delay

In the wake of the U.S. Supreme Court's decision in FTC v. Actavis,[3] which held that settlement payments from a branded drug company to a generic to delay the launch of a generic drug may raise antitrust concerns, the number of reverse payment settlements dropped significantly.[4] However, Actavis did not put an end to the many legal questions surrounding these pay-for-delay agreements.

Pharmaceutical companies continue to invent new ways to compensate generic rivals for staying out of the market for certain branded drugs without providing a large, cash payment. Side deals such as authorized generic (AG) relationships and "No-AG" clauses are just two of the ways branded firms can provide financial incentives to a generic competitor to delay a generic product's commercial release. Establishing collaborative agreements for products other than those in-suit may also help innovator and generic firms to hide the ball from antitrust enforcement. Meanwhile, courts have struggled to adapt and stem new tides of anti-competitive conduct. Recognizing that settlements containing lucrative contracts may be tantamount to a large cash payment, the First Circuit overturned a lower court's

finding that Actavis applied "only to cash settlements or to their very close analogues"[5] and expanded the holding in Actavis to noncash forms of settlement payments.[6]

Eliminating harmful pay-for-delay arrangements entirely would require clarification of federal law. Currently, the FDA's capacity to unilaterally address the pay-for-delay problem is limited by the scope of its authority to grant regulatory exclusivity. However, just as the FDA may approve extensions of exclusivity under certain circumstances, so too might the FDA gain the ability to revoke exclusivity to punish or deter pay-for-delay arrangements. Because the agency already actively reviews applications for generic drugs, it is well positioned to detect where a settlement produces adverse results for the public, and to take regulatory actions to penalize pharmaceutical firms that would put short-term profits ahead of consumer welfare.

Product Hopping

"Product Hopping" or "switch" is a tactic whereby a drug innovator produces a modest reformulation of an existing product, offering little or no therapeutic advantage, in the eleventh hour before the release of a competing generic.[7] If enough patients switch to the new formulation, the switch forces a generic competitor to go back to the drawing board and develop a drug bioequivalent to the new formulation, at which point the innovator can release a subsequent reformulation, ad infinitum.

Even when a product hop serves as a thinly veiled pretext to diminish the impact of generic competition, the conduct is not an easy target for antitrust enforcement. Mistakenly condemning product changes driven by consumer demand or pursuit of safer alternatives, could deter valuable innovation.[8]

Both the FTC and private plaintiffs have filed suits to deter harmful product hops, but the FDA's participation in the controversy has been comparatively minimal. However, the FDA's central role in overseeing clinical trials for efficacy and safety make it particularly well-suited to distinguish anti-competitive hops aimed at impeding competitors from genuine improvements to a drug formulation. Accordingly, the FDA is well equipped to increase its involvement or play an advisory role to assist the enforcement of the FTC or private plaintiffs.

Improper Listing

Historically, drug innovators have found ways to manipulate FDA Orange Book listing procedures to the detriment of generic competitors. Capitalizing on the FDA's self-proclaimed ministerial role in patent law, drug innovators have listed inapplicable patents or use codes to erect new barriers to prevent generic competitors from completing their abbreviated new drug applications.

The Busiprone Antitrust Litigation case serves as a prime early example of improper listing. In that case, defendant Bristol-Myers Squibb Co. submitted a patent to the FDA to be listed alongside its anti-depressant BuSpar on the eve of the expiration of BuSpar's primary existing patent. In response to the new listing, the FDA halted its review of pending ANDA filings. A subsequent infringement suit triggered Hatch-Waxman's 30-month stay and further delayed approval of a generic alternative. The suit also revealed that neither the Hatch-Waxman Act nor FDA regulations contained a mechanism for a competitor to petition for removal of a patent from the Orange Book.

Congress swiftly responded through new legislation to provide a counterclaim in a Hatch-Waxman infringement action to "correct or delete" certain patent information blocking ANDA approval.[9]

However, Congress' solution did not put an end to improper listing strategies.

Nearly a decade later, in Caraco v. Novo Nordisk, drug innovator Novo Nordisk amended its labeling information, specifically, a use code, for its diabetes treatment to impede the release of a competing generic. This time, the law provided no mechanism to correct the improperly listed code. The Supreme Court intervened to fill the gap and held that the MMA counterclaim to delist improper patents was also available to amend labeling information such as use codes.

In a concurring opinion, Justice Sonia Sotomayor predicted that the counterclaim would not suffice to put an end to abusive Orange Book listings. Moreover, Justice Sotomayor admonished the FDA for "rel[ying] on use codes in determining whether to approve an ANDA, but [refusing] to evaluate the accuracy of those codes."[10]

In the notice for the FDA's meeting, the FDA specifically requested commentary on how Hatch-Waxman's balance between innovation and access has been affected by patents, including patent listing procedures.[11] However, it remains unclear how the agency would address these patent listing issues without taking a more active role in substantively reviewing patents. Alternatively, the FDA could seek to improve its oversight of listed patents through collaborative efforts with other administrative experts, such as the United States Patent and Trademark Office.

Citizen Petitions

Congress permits individuals to express genuine concern about product safety to the FDA before or after a product enters the market by a mechanism called a citizen petition.[12] Filed on or near the time a generic prepares to enter the market, the petition can disrupt generic approvals by forcing the FDA to evaluate the petitioner's arguments.

Despite the anti-competitive impact of this practice, the Noerr-Pennington doctrine, which immunizes attempts to influence government to policies with anti-competitive consequences,[13] is frequently employed by brand-name pharmaceutical firms to shield these anti-competitive efforts from antitrust liability.[14]

On Feb. 7, 2017, the FTC filed a first-of-its-kind lawsuit against Shire ViroPharma Inc.,[15] alleging that Shire violated antitrust laws via "a campaign of serial, repetitive, and unsupported filings with the U.S. Food and Drug Administration and Courts," to delay approval of generic versions of Shire's antibiotic.[16]

Although the FDA is not required to respond to a citizen petition before it approves a related ANDA, its public safety mission more often than not prevents approval while a citizen petition is pending, and an artfully drafted petition may survive antitrust scrutiny if it sufficiently implicates issues of public health.[17]

In the high cost industry of pharmaceutical sales, even short delays can cost generic firms millions in lost sales. More importantly, delays may bring uncertainty to patients requiring access to treatments and will inevitably lead to overpayment for branded prescription drugs in the absence of generic alternatives. As the FDA begins to address problems with consumer access to affordable therapies, its stance on citizen petition review may be first on the list. In fact, in the agency's announcement for its July 18 meeting, the FDA requested stakeholder input on regulatory processes including the citizen petition process.

REMS-Based Refusals to Deal

The creation of risk evaluation and mitigation programs added a new tool in the belts of innovator firms attempting to forestall generic competition.

At the discretion of the FDA, a branded company sponsoring a new drug application may be required to implement a risk evaluation and mitigation strategy (REMS) program as a precondition to NDA approval. REMS give the FDA greater post-approval authority over drugs to ensure that a drug's benefits continue to outweigh its risks. REMS requirements may include: distribution restrictions; training and record-keeping requirements for prescribers and pharmacists; and prescribing limitations.[18]

Drug innovators wasted no time in deploying REMS strategies to refuse to sell product samples to generic manufacturers, thereby precluding a rival firm from formulating a generic. Just two years after Congress granted the FDA authority to impose REMS, generic manufacturers began to complain that a major branded firm refused to sell samples of two high-toxicity drugs subject to REMS distribution requirements.[19]

A study published in July 2014 estimated that the delayed release of generics resulting from abuse of REMS distribution restrictions led to annual overspending of $5.4 billion on pharmaceuticals.[20] However, curtailing abusive REMS practices will not come without challenges.

Congress, when it granted the FDA authority to impose REMS, expressly prohibited innovator firms from using REMS as anti-competitive tools to block generic competition.[21] However, its legislative mandate failed to specify penalties for abuse or provide a private right of action. Although the FDA is in the best position to manage unintended consequences these regulations, its statutory grant of authority provides minimal guidance on its enforcement capabilities. Furthermore, the FDA's overall institutional goal, which frequently places safety ahead of innovation, has so far impeded agency action in this area.

That may soon change, as both FDA Director Scott Gottlieb and numerous public commentators have already highlighted changes to REMS regulations as a prime area for agency action as the FDA embarks on its new price-minded agenda. Dr. Gottlieb specifically criticized abusive REMS practices, which undermine Hatch-Waxman's dual objectives of promoting drug innovation and improving patient access. Consequently, the FDA has explicitly sought feedback as to what additional actions the agency should take, within its legal authority, to reduce delays in access to product samples that generic companies often face when preparing generic approval applications.

Conclusion

In passing the Hatch-Waxman Act, Congress recognized the importance of rewarding innovation in the pharmaceutical industry with temporary market exclusivity to promote scientific advancement and provide drug innovators with a means to defray their substantial research and development costs. However, in the three decades since the act's inception, the complexity of the regulatory process has disguised anti-competitive activities that hinder consumer access to lower-cost generic treatments. The FDA has embraced its role as a protector of public safety while also promoting patient access to needed therapies. At the FDA's recent public meeting on the Hatch-Waxman amendments, Director Scott Gottlieb announced the agency's new "Drug Competition Action Plan," an initiative designed to curb the anti-competitive "gamesmanship" practiced by drug manufacturers that leads to inflated drug prices. While the agency will undoubtedly tighten its standard operating procedures as part of this initiative,

the agency may also extend its efforts to areas that it has consciously avoided for years. For example, the FDA may begin its Action Plan by exercising existing statutory authority to curtail abuses of REMS requirements or the citizen petition process. Meanwhile, the FDA may venture into new territory to oversee patent listings or scrutinize drug reformulations that serve as veiled attempts to "product hop." As the agency works to address anti-competitive end-runs around its regulations, players in the pharmaceutical industry must walk a fine line between risking antitrust liability and protecting their revenue streams.

The FDA is accepting public comments until Sept. 18, 2017, at Docket No. FDA-2017-N-3615.

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[1] 21 C.F.R. §§ 314.108, 316.31, 316.34; Food Drug and Cosmetic Act, 21 U.S.C. §§ 505A-E, 505(j)(5)(B)(iv).

[2] Press Release, FDA Working to Lift Barriers to Generic Drug Competition, Food & Drug Admin. (June 21, 2017).

[3] Federal Trade Commission v. Actavis, Inc., et al., 133 S. Ct. 2223 (2013).

[4] See Diane Bartz, Controversial 'pay-for-delay' deals drop after FTC's win in top court, Reuters (Jan. 13, 2016 2:20 PM).

[5] In re Loestrin 24 Fe Antitrust Litig., 45 F.Supp.3d 180, 192 (D.R.I. 2014).

[6] In re Loestrin 24 Fe Antitrust Litig., 814 F.3d 538, 549 (1st Cir. 2016).

[7] Press Release, FTC Files Amicus Brief Explaining That Pharmaceutical "Product Hopping" Can Be the Basis for an Antitrust Lawsuit, Fed. Trade Comm'n, (Nov. 27, 2012), https://www.ftc.gov/news-events/press-releases/2012/11/ftc-files-amicus-brief-explaining-pharmaceutical-product-hopping

[8] Jessie Cheng, Note, An Antitrust Analysis of Product Hopping in the Pharmaceutical Industry, 108 Colum. L. Rev. 1471, 1504 (2008).

[9] Medicare Prescription Drug, Improvement, and Modernization Act, 42 U.S.C. § 1301 (2003).

[10] Caraco Pharm. Labs, Ltd. V. Novo Nordisk A/S et al., No. 10-844, 566 U.S. ___, slip op. at 25 (Apr. 17, 2012).

[11] Dep't of Health & Human Servs., Food & Drug Admin., Administering the Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access; Public Meeting; Request for Comments, Docket No. FDA-2017-N-3615 (July 14, 2017).

[12] 21 C.F.R. 10.30; Federal Food, Drug, and Cosmetic Act (FDCA), § 505(j), 21 U.S.C. §§ 335(j).

[13] Noerr-Pennington immunity shields a party's good-faith efforts to elicit favorable government action even if the purpose or consequence of those efforts brings about anticompetitive effects. See Eastern Railroad Presidents Conference v. Noerr Motor Freight, Inc., 365 U.S. 127, 136 (1961); United Mine Workers v. Pennington, 381 U.S. 657, 670 (1965).

[14] See, e.g., Michael A. Carrier & Daryl Wander, Citizen Petitions: An Empirical Study, 34 Cardozo L. Rev. 249, 263 (2012) (describing brand-name pharmaceutical companies' deployment of citizen petitions as an anticompetitive delaying tactic to impede generic drug competition).

[15] Fed. Trade Comm'n . Shire ViroPharma Inc., No. 17-00131 (D. Del. filed Feb. 7, 2017).

[16] See Press Release, FTC Charges That Shire ViroPharma Inc. Abused Government Processes Through Serial, Sham Petitioning to Delay Generics and Maintain its Monopoly over Vancocin HCI Capsules, Fed. Trade Comm'n (Feb. 7, 2017).

[17] See Carrier & Wander, supra note 12, at 281.

[18] Food and Drug Administration Amendments Act of 2007, 21 U.S.C. 301, Pub. L. 110-85 (as amended by Pub. L. 110-316). FDCA §§505(p), 505-1 (2014)/21 U.S.C. §§355(p), 355-1 (2014). See Food and Drug Admin., Approved Risk Evaluation and Mitigation Strategies (REMS), http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm (last visited July 17, 2017).

[19] Food and Drug Admin., Thalomid (thalidomide) REMS, NDA # 020785 (Initial REMS Approved Aug. 2010; Most Recent Modification Nov. 2013), http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM222649.pdf (last visited July 15, 2017).; Food and Drug Admin., Revlimid (lenalidomide) REMS, NDA # 021880 (Initial REMS Approved Aug. 2010; Most Recent Modification Nov. 2013), http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM222644.pdf (last visited July 15, 2017).

[20] Alex Brill, Matrix Global Advisors, Lost Prescription Drug Savings from Use of REMS Programs to Delay Generic Market Entry, Generic Pharm. Ass'n (July 2014).

[21] "No holder of an approved covered application shall use any element to assure safe use required by the Secretary under this subsection to block or delay approval of an application under § 355 (b)(2) or (j) of this title or to prevent application of such element under subsection (i)(1)(B) to a drug that is the subject of an abbreviated new drug application." 21 U.S.C. § 355-1(f)(8).
