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-- Expert Paper by Scott Hemphill --

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Unjustified Delays in Generic Drug Competition

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This short paper discusses collusive and unilateral conduct by drug makers that delays the entry of less expensive generic drugs. The chosen examples are illustrative, not exhaustive. The analysis focuses on the U.S. experience, with a view to informing the work of competition authorities in other jurisdictions. The paper considers several theories of liability, presents responses of defendants, and suggests one avenue of proactive enforcement.

1. Background

Innovative new drugs have made a major contribution to longer, healthier lives. For most new drugs, a branded drug maker's exclusive right to market a new drug is protected, for a period of time, by a combination of patents and non-patent regulatory protection. The firm's expectation of exclusivity provides an incentive to innovate, thereby justifying large investments in research and clinical testing. The resulting profits also promote innovation by supplying the funding for future research and testing, to the extent that such investments are funded out of current cash flows, rather than capital markets.

Upon loss of exclusivity, cheaper generic drugs enter the market. In 2013, generic drugs accounted for 86 percent of U.S. prescriptions but just 29 percent of drug expenditures, which reached a new peak of \$329 billion.¹ Generic drugs saved the U.S. health system more than \$200 billion in 2012, according to an industry commissioned study.² Robust competition from generic drugs is thus a powerful source of lower prices.

One important determinant of the duration of exclusivity is the nature and extent of patent protection. In the United States, the 1984 enactment of the Hatch-Waxman Act set up a legal framework for generic entry. Under rules created by the Act, a generic firm must wait until

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¹ IMS Institute for Healthcare Informatics, *Medicine Use and Shifting Costs of Healthcare: A Review of the Use of Medicines in the United States in 2013*, at 30, 40 (2014).

² Generic Pharmaceutical Association, *Generic Drug Savings in the U.S.* (2013).

patent expiration or else assert that one or more patents are invalid or not infringed. That assertion is an act of patent infringement, which typically prompts the branded firm to file a lawsuit to prevent the generic firm's product launch. The outcome of that suit—including a settlement—determines when the generic firm can enter the market.

Since 1984, branded firms have substantially stepped up their patenting efforts in a bid to postpone the loss of exclusivity. Patents per drug roughly doubled for the cohort of U.S. drugs approved between 2000 and 2002, compared with drugs approved between 1985 and 1987.³ Multiple patents with overlapping terms result in a longer nominal term of protection. In Europe, the trend is similar.⁴ Part of this growth reflects a rise in secondary patents. These provide regulatory protection to ancillary aspects of drug innovation—such as particular drug formulations and compositions—beyond the core, traditional protection, a patent on a novel active ingredient. At the same time, secondary patents, particularly late-expiring ones, are disproportionately targeted for pre-expiration challenge by generic firms.⁵

None of this, in itself, raises antitrust concern. Asserting a patent against a generic firm is a legitimate source of delayed entry, part of the incentive to innovate provided to a branded firm. But neither does patent law trump antitrust. Antitrust concerns should not be dismissed on the ground that higher brand profits promote innovation. Such an argument proves too much, granting immunity even to price fixers in innovative industries. A further issue is that purchasers in a lenient jurisdiction would thereby bear a disproportionate burden, through higher prices, in supporting innovation that brings global benefit. In the United States, the idea that patent trumps antitrust as a matter of law or policy has been decisively rejected by the U.S. Supreme Court.⁶

Taken together, the patent and regulatory rules governing generic entry set a balance between low-price access to existing drugs and preservation of the incentive to develop new drugs. Unjustified delays in the onset of generic competition are cognizable anticompetitive harms because they prolong the period of high profits and prices enjoyed by a branded firm, beyond the point of balance set by these rules. These delays can occur through the coordinated activity of several drug makers, or by a branded firm acting alone. These concerns are

³ C. Scott Hemphill & Bhaven N. Sampat, When Do Generics Challenge Drug Patents?, 8 *Journal of Empirical Legal Studies* 613 (2011). The analysis compares patents listed in the Orange Book, which excludes some pertinent patents.

⁴ European Commission, *Pharmaceutical Sector Inquiry Final Report* (2009).

⁵ C. Scott Hemphill & Bhaven N. Sampat, Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals, 31 *Journal of Health Economics* 327 (2012).

⁶ *Federal Trade Commission v. Actavis, Inc.*, 133 S. Ct. 2223 (2013).

considered in the next two sections, which lay out several theories of liability and responses of defendants.

2. Collusive Conduct

2.1 Reverse Payment Settlements

One source of delayed generic entry, the subject of more than fourteen years of antitrust litigation in the United States, is so-called “reverse payment” settlements of patent litigation between branded and generic drug makers. Reverse payment settlements have two essential elements: a large payment from the branded firm to the allegedly infringing generic firm, and a requirement that the generic firm refrain from competing in some respects for a period of time. In June 2013, the U.S. Supreme Court recognized that reverse payment settlements can violate antitrust law.⁷ One year later, plaintiffs are pursuing reverse payment litigation as to at least 18 drugs (see Table 1).

Table 1. Reverse Payment Litigation in the United States

Year of first settlement	Active ingredient (brand name)
1997	Ciprofloxacin (Cipro)
2005	Potassium chloride (K-Dur)
	Metaxalone (Skelaxin)
	Modafinil (Provigil)
	Niacin (Niaspan)
	Lamotrigine (Lamictal)
2006	Venlafaxine (Effexor XR)
	Mixed amphetamine salts (Adderall XR)
	Testosterone (Androgel)
2007	Bupropion (Wellbutrin XL)
2008	Atorvastatin (Lipitor)
	Aspirin and dipyridamole (Aggrenox)
	Esomeprazole (Nexium)
	Minocycline (Solodyn)
2009	Norethindrone and ethinyl estradiol (Loestrin)
2010	Pioglitazone (Actos)
	Pioglitazone and metformin (Actoplus met)
2012	Lidocaine (Lidoderm)

⁷ Id.

A mere compromise on entry dates is not a form of payment and does not raise antitrust concern. In ordinary brand-generic patent litigation, late entry dates are bad for drug purchasers, but also bad for the generic firm. Generic profits are a function of the amount of time on the market. The generic firm therefore can be expected to fight for an earlier entry date. That alignment of interests between the generic firm and purchasers is maintained in a compromise over entry dates. The resulting outcome of litigation or settlement is a legitimate consequence of the protection from competition provided by a patent.

Matters are different when the branded firm relies not only on the inherent force of the patent, but on a payment as well. The payment secures less competition than the branded firm could expect by asserting the patent alone in litigation or settlement. The payment, in other words, is for *additional* generic delay, compared to what is legitimately achieved by the patent alone.

The basic theory of liability recognized by the Supreme Court does not depend on any general intuition or case-specific finding that the generic firm would likely have won the patent suit. The key to the antitrust case is an inference of anticompetitive effect from the observed facts of a large payment plus delayed entry. Whether the branded firm would likely win or lose, the payment disrupts the alignment of interest between the generic firm and drug purchasers. The generic firm is compensated for accepting the delay, but purchasers are not.

Nor does the basic theory depend on the peculiarities of the U.S. regulatory scheme. Under the Hatch-Waxman Act, the first generic firm to challenge a branded drug's patents is eligible for a 180-day exclusive right to market in competition with the branded firm, before other generic firms may enter. The generic exclusivity period is certainly relevant, by encouraging patent challenges in the first place and by furnishing an entry-delaying inducement to settle, but it is not an essential feature of reverse payment settlements. In the United States and other jurisdictions, challenges and reverse payment settlements occur without relying on exclusivity.

2.2 Responses of Defendants

In these cases, defendants have made a number of responses that are likely to recur in other jurisdictions.

[1] *No cognizable payment.* Defendants argue that particular forms of alleged compensation, which do not take the form of cash, are not cognizable. These include:

- the forgiveness of patent infringement damages or other debt owed by the generic firm to the branded firm;
- a “sweetheart” deal on goods or services purchased by the generic firm from the branded firm; and
- a branded firm’s abstention from vigorous competition once the generic firm enters the market, thereby lowering brand profits and increasing generic profits.

Plaintiffs counter that the anticompetitive effect of payment transcends its particular form.

Several U.S. cases have considered a version of the latter form of payment, in which the branded firm agrees not to market its own unbranded (“authorized”) generic product in competition with the generic firm. Such “no authorized generic” deals not only transfer value but also preserve a less competitive market structure. This mutual forbearance from competition thus poses a competitive threat, above and beyond the usual reverse payment case.

[2] No net payment. In cases where cash flows from the branded to the generic firm, defendants offer a second response. Defendants describe the payments as consideration for value furnished by the generic firm as part of the settlement, rather than delay. The asserted value takes various forms, including drug promotion, backup manufacturing services, and intellectual property licenses. Such settlement provisions raise the questions of how to establish a net payment, and whose responsibility it is to do so. In seeking to place some or all of the responsibility on defendants to show that the payment was for services, not delay, plaintiffs point to the fact that such deals are rare outside the context of settlement.

[3] Risk avoidance and risk aversion. Defendants argue that settlement should be permitted because the parties have a natural or inevitable preference to avoid the risk of losing the litigation. This “litigation risk” argument reflects the understandable appeal of settlement and widespread dislike of patent litigation. That said, some of these arguments amount to an aversion to competition, which is the premise for liability, rather than a defense. Plaintiffs have thus responded that certainty is not a virtue that may be purchased at the expense of prolonging monopoly.

A more sophisticated defense relies on risk aversion by the branded firm. Risk aversion is not a mere dislike of competition, but a willingness to pay to avoid a gamble with the same expected value. A risk-averse branded firm, in order to avoid the gamble of litigation, might therefore accept a no-payment settlement with an earlier entry date, with the consequence that consumers enjoy more competition under the settlement than they could expect from litigation. Rather than simply agree to an early no-payment settlement, however, the risk-

averse branded firm (if permitted) could make a reverse payment to the generic firm, in exchange for later entry.

In theory, a settlement with a reverse payment undertaken by a risk-averse branded firm might be better or worse for consumers than litigation. However, such settlements are still anticompetitive, compared to a feasible no-payment settlement with an early entry date.⁸ Moreover, even if a hypothetical settlement with payment and an earlier-than-litigation entry date is feasible, it is unlikely to be chosen, given the parties' shared incentive to choose a settlement with a larger payment and later entry date.⁹

[4] *A strong patent.* Some defendants focus on the patent at issue in the settled litigation, asserting that it was strong. They might buttress that assertion with detailed technical evidence or internal analyses indicating that the patent was valid and infringed. Such evidence might be thought valuable by identifying the expected amount of competition absent the settlement, providing a baseline that could then be compared to the terms of the settlement. If the patentee were sufficiently likely to have won the patent case, then (a defendant might argue) a settlement with a particular entry date provides at least as much competition as the expected outcome of patent litigation.¹⁰ Plaintiffs might do the opposite, presenting evidence that the generic firm would have won the patent case, and hence that the settlement is anticompetitive.

This patent-focused approach provides an alternative to the payment-based inference emphasized by the Supreme Court. The Court was at pains to discourage this alternative, noting that a patent mini-trial inside the antitrust case would be "time consuming, complex, and expensive."¹¹ A less complex alternative would be to take a step back from the particular patent, and evaluate the likelihood of success using basic information about the type or class of patents. For example, does the patent at issue cover the active ingredient? In U.S. patent litigation, the branded firm nearly always wins suits asserting such patents.¹² Such evidence, on this view, would tend to establish a defense for reverse payment settlements involving active ingredient patents. By contrast, the branded firm usually loses suits asserting secondary

⁸ Under yet additional assumptions, a no-payment settlement is infeasible.

⁹ For further discussion, see Aaron Edlin, Scott Hemphill, Herbert Hovenkamp, and Carl Shapiro, *Actavis and Error Costs* (working paper 2014).

¹⁰ An analogous approach is to argue that the generic firm could not have entered the market in any event due to manufacturing difficulties that independently prevented regulatory approval.

¹¹ *Federal Trade Commission v. Actavis, Inc.*, 133 S. Ct. 2223, 2233 (2013).

¹² C. Scott Hemphill & Bhaven N. Sampat, *Drug Patents at the Supreme Court*, 339 *Science* 1386 (2013) (reporting, for a dataset of completed patent litigation on all drugs that first became eligible for challenges between 2000 and 2008, a 92 percent branded success rate for active ingredient patents).

patents.¹³ This approach would tend to establish liability in reverse payment settlements about secondary patents.

2.3 Collusion Among Generic Drug Makers

Collusion among generic firms can also impede competition. The price of drugs is affected not only by the fact of generic entry, but also its extent. The price drop from generic entry is modest with one generic competitor, and increases with additional entrants. Moreover, generic profits fall with additional generic entry. A generic drug maker thus has an incentive to impede additional entry and thereby prolong high prices.

One alleged example is a deal between Teva and Ranbaxy. In 2010, the two generic drug makers negotiated the terms of generic entry for atorvastatin (Lipitor), a blockbuster statin. One term of the agreement pertained to the 180-day regulatory exclusivity discussed above. In the United States, generic firms frequently challenge one another's eligibility for exclusivity. A successful challenge permits additional generic firms to enter the market sooner. In the agreement, Teva and Ranbaxy agreed not to challenge one another's exclusivity, as to Lipitor and many other drugs. The potential effect, according to the New York Attorney General, was to impede successful challenges to exclusivity. The NYAG secured a consent decree nullifying this term and prohibiting its recurrence.¹⁴

3. Unilateral Conduct

3.1 Product Hopping

Generic entry may also be impeded by the unilateral conduct of a branded firm. The most prominent current issue relates to line extensions of existing products. Branded firms frequently develop or acquire new versions of an existing drug, including new dosage forms (for example, a tablet instead of a capsule), extended release formulations, and more potent chemical variants such as stereoisomers. They may also develop (or acquire¹⁵) alternative therapies in the same therapeutic class. Line extensions often involve significant improvements

¹³ Id. (reporting a 32 percent success rate for secondary patents).

¹⁴ New York Attorney General, Assurance of Discontinuance No. 14-034 (Feb. 12, 2014).

¹⁵ The acquisition of a substitute therapy may violate antimerger law, apart from any product hopping concerns. For example, in *Federal Trade Commission v. Lundbeck, Inc.*, 650 F.3d 1236 (8th Cir. 2011), the FTC sued to enjoin an acquisition that brought together two branded drugs that treat patent ductus arteriosus. The challenge was rejected on the ground that the FTC had failed to define a relevant market.

over the original, leading some patients and doctors to prefer the new drug. The mere introduction of a new and improved product raises no antitrust concern.

Where the new product has stronger or longer-lived exclusivity, the branded firm has an incentive to shift patients and doctors from the old product to the new one. A “product switch” or “product hop” can be accomplished in various ways, including promoting the new product, increasing the relative price of the old product, withdrawing inventory of the old product, and withdrawing regulatory approval of the old product. A successful hop leaves the generic drug, once approved, with relatively few customers. The effect is particularly pronounced when law or commercial practice permits or requires substitution of the branded product.

Product hopping can harm drug purchasers who pay a higher price for a therapy of equal or even lesser quality. In considering antitrust liability, three issues bear particular note. First, is the new product no better than the old? In an extreme case, the change might have the sole effect of creating an incompatibility between the new exclusive product and the old genericized product that avoids competition. Second, were customers forced to make a switch? Product withdrawal is more successful, but also more troubling, when it is accomplished prior to approval of the generic version, thereby denying patients the choice of an existing therapy that works well for them.

Third, are some existing patients harmed by the switch? For some patients, the new therapy may be of lower quality. For example, use of the new therapy might reduce compliance or produce new adverse side effects, results that the branded firm causes by depriving the patient of the old product. This is a further harm, in addition to the prolonged period of high prices.

3.2 Responses of Defendants

[1] Product design is privileged. Defendants have responded that product design decisions are generally not subject to antitrust scrutiny. Innovators have significant latitude to develop and market new products. Courts are properly skeptical of claims that a purported innovation has actually harmed consumers. But not every claim of innovation is entitled to deference, particularly where incompatibility is achieved without product improvement.¹⁶

Moreover, even if product design is privileged, the withdrawal of an existing product may not be. U.S. doctrine reflects this distinction. In a leading U.S. case that otherwise

¹⁶ United States v. Microsoft Corp., 253 F.3d 34, 65 (D.C. Cir. 2001) (en banc) (per curiam) (product design decisions are not per se lawful).

celebrates an innovator's latitude in product design decisions, the court added the proviso that this latitude existed "so long as free choice of consumers is preserved," noting in dicta that if the innovator had withdrawn the old product, the loss of consumer choice would present a more troubling case.¹⁷

[2] *No cognizable loss of competition.* Defendants argue that product hopping results in no cognizable loss of competition. When the generic firm enters the market, it is free to sell its version of the old product in competition with the new branded product. If the old product is desirable, it will garner significant sales; if not, that merely demonstrates that the new product is indeed an improvement. To be sure, the generic product misses out on the boost from the branded firm's active participation in the market, but on this view, antitrust does not require such solicitude. On the other hand, such free-riding by the generic firm may be central to the competition set up by the regulatory scheme. Moreover, this defense argument does not apply to patients who are immediately harmed upon product withdrawal, before the generic version becomes available.

3.3 Manipulation of the Patent and Regulatory Regimes

Other unilateral conduct takes the form of manipulation of the patent system, either in the improper acquisition of the patent or its improper assertion in litigation.¹⁸ Patent improprieties may be compounded by misuse of the regulatory system. The specific form of such abuse necessarily varies, given differences among jurisdictions. For example, in the United States, the improper listing of a patent in a regulatory publication called the Orange Book can trigger a multiyear delay in regulatory approval during the pendency of a subsequent patent suit.

Other forms of "gaming" do not depend on the patent system. For example, an incumbent may file a so-called "citizen's petition" with the regulatory approval agency, raising doubts about the approvability of a proposed generic product, simply in order to delay entry. Or it might exploit regulatory procedures that restrict the public availability of a dangerous or addictive drug, in order to deny a generic firm the samples it needs to prepare an approvable bioequivalent product.

¹⁷ *Berkey Photo, Inc. v. Eastman Kodak Co.*, 603 F.2d 263, 287 & n.39 (2d Cir. 1979).

¹⁸ See, e.g., *In re DDAVP*, 585 F.3d 677 (2d Cir. 2009).

4. Conclusion

Collusive and unilateral efforts to delay generic drug entry continue to attract attention from competition authorities. Well-chosen enforcement actions play a crucial role in curbing anticompetitive conduct, and thereby maintaining an appropriate balance between innovation and access. Beyond enforcement in individual cases, authorities might wish to consider a more proactive stance.

One promising option is to focus on weak patents—weak, in the sense that a court is unlikely to conclude that they are valid and infringed by a competing generic product. The granting of weak, late-expiring patents is a necessary condition or facilitator for much of the conduct discussed in this paper. Weeding out these patents in the first place would reduce the opportunity for anticompetitive conduct. Although careful early evaluation of all patents in all fields may not be worth the trouble, screening might nevertheless be desirable for all drug patents, a much smaller set. One indicator of scale is that only about 300 to 400 new patents are added to the Orange Book each year.

A wide range of tools are available, including robust post-grant opposition procedures, state-sponsored challenges, and “bounties” for successful invalidation or cancellation by private parties. This proposal is hardly a panacea, as it affects only those patents that are weak because they are invalid, as opposed to narrow and therefore easily invented around. And it is important to make sure that a proposed solution does not spawn new problems. Perhaps the most prominent existing example of a bounty is the 180-day exclusivity. That U.S. provision has proven susceptible to manipulation, indicating the importance of careful regulatory design.¹⁹

¹⁹ See C. Scott Hemphill, *An Aggregate Approach to Antitrust: Using New Data and Rulemaking to Preserve Drug Competition*, 109 *Columbia Law Review* 629 (2009); C. Scott Hemphill & Mark A. Lemley, *Earning Exclusivity: Generic Drug Incentives and the Hatch-Waxman Act*, 77 *Antitrust Law Journal* 947 (2011).