Report from North America

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PATENT SETTLEMENTS IN THE PHARMACEUTICAL INDUSTRY: BALANCING INTELLECTUAL PROPERTY AND ANTITRUST CONCERNS

Introduction

Patent settlement agreements can significantly influence the competitive environment of an industry. In recent years, patent settlement agreements in the US pharmaceutical industry have received a great deal of attention from economists, antitrust authorities, and the courts.[1] The agreements at issue have arisen under a regulatory framework introduced by the Hatch-Waxman Amendments to the *Federal Food, Drug, and Cosmetics Act 1938*, which, among other things, aimed to make available more low cost generic drugs. In some cases, these settlement agreements have provided for payments from the branded manufacturer to the generic manufacturer in exchange for the generic manufacturer agreeing to remain out of the market until the litigation is resolved. The very different treatment of two similar agreements of this type in recent months – by the Sixth Circuit (which ruled that these agreements are per se violations of s 1 of the *Sherman Act 1890*) and Eleventh Circuit Court of Appeals (which ruled that these agreements should be analysed using a rule of reason approach) – demonstrates the complexity of balancing the benefits of innovation and the potentially anticompetitive effects of these settlement agreements. While these agreements may reduce competition in the short run, they can lower the costs of enforcing valid patents and protect incentives for firms to innovate in the long run. To protect potentially procompetitive agreements, a rule of reason approach is more appropriate.

The Hatch-Waxman Amendments and Paragraph IV certification

The US FDA approval process

In the US, a company seeking to market a new drug must obtain approval from the US Food and Drug Administration (FDA). Since 1962, the FDA has required pharmaceutical companies to prove that new brand name and generic drugs are "safe and effective" prior to approval, by conducting costly clinical trials.[2] In addition, generic companies could not begin such research until patents on the brand-name drug expired, lest they risk a patent infringement suit. As a result, the approval process effectively extended the life of the branded companies' patents and deterred generic entry.

In 1984, the US Congress passed the Hatch-Waxman Amendments (Hatch-Waxman) to the *Federal Food, Drug, and Cosmetics Act 1938*, which sought to balance branded pharmaceutical companies' incentives for innovation with generic pharmaceutical companies' opportunities for market entry. Among other things, Hatch-Waxman streamlined the approval process for generic manufacturers, thereby reducing the costs of obtaining FDA approval and speeding the time to market.

More specifically, Hatch-Waxman allowed generic pharmaceutical companies to submit an Abbreviated New Drug Application (ANDA), simply referencing the safety and efficacy results submitted by the branded company rather than including results of clinical trials specifically for the

[1] See, for example, Langenfeld J and Li W, "Intellectual Property and Agreements to Settle Patent Disputes: The Case of Partial Settlement Agreement with Payments from Branded to Generic Drug Manufacturers" (2002) 70(3) *Antitrust Law Journal* 777 at 777-818; Shapiro C, "Antitrust Limits to Patent Settlements" (2003) 34(2) *RAND Journal of Economics* 391 at 391-411; "Generic Drug Entry Prior to Patent Expiration: An FTC Study" (July 2002) at http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf viewed 27 May 2004.

[2] The lengthy FDA approval process often shortened the effective life of brand-names companies' patents when approval was received *after* the patent was granted.

generic drug, so long as the generic drug could demonstrate "bioequivalence" to the relevant brand name drug.[3] In addition, the ANDA applicant must certify one of the following:

(I) the required patent information has not been filed;

(II) the patent has expired;

(III) the patent will expire, identifying the expiration date; or

(IV) the patent is invalid and/or not infringed.

The latter representation is known as a Paragraph IV certification.

Paragraph IV certification

An ANDA filer who makes a Paragraph IV certification must notify the patent holder of the basis for their assertion of patent invalidity or non-infringement. Under Hatch-Waxman, if a patent-holder files suit within 45 days of the filing of a Paragraph IV certification, the branded company is granted an automatic "stay" of FDA approval of the generic company's ANDA until the earliest of: (1) 30 months from the notification date; (2) the court decides the patent is invalid or not infringed; or (3) the patent expires.[4] This is commonly known as a "30 month stay," which effectively extends the life of the patent and compensates the innovator for time lost during its approval process.[5]

Another key provision of Hatch-Waxman is that the first generic pharmaceutical company to file an ANDA with a Paragraph IV certification is awarded a "180-day exclusivity period," during which time the FDA may not approve any ANDAs filed subsequently for the same drug. The exclusivity period begins on the earlier of the date of the first commercial marketing of the generic drug or the date of a court decision holding the patent invalid or not infringed. The 180-day period of exclusive marketing provides generic firms with additional incentive to challenge potentially invalid patents or to invent around the patented technology by developing a non-infringing alternative.

Patent settlement agreements in the pharmaceutical industry

In recent years, an increasing number of generics have sought to enter the market before the expiration of a branded drug's patent(s), by filing a Paragraph IV certification. Associated with that has been an increase in patent litigation. Since 1992, at least 20 final settlement agreements (where the agreement settled the litigation) and four interim settlement agreements (where the agreement did not completely settle the litigation, but governed conduct in the interim period) have been filed.

Final settlement agreements typically specify a date for future generic entry. Interim settlement agreements, by comparison, typically involve an agreement by the generic company to stay off the market until the end of the litigation (even if the litigation lasts beyond the 30-month stay, and the generic drug is approved by the FDA in the interim) in exchange for a payment from the branded company. In addition, interim agreements have stipulated that the generic cannot relinquish its 180-day exclusivity period (which doesn't begin until the generic company begins marketing its drug), therefore ensuring that other generic manufacturers cannot get FDA approval until the litigation is resolved.[6]

Because these agreements may have the effect of keeping a low-priced generic drug off the market temporarily, they have been challenged by both US antitrust authorities and private plaintiffs. In the late 1990s, the FTC began investigating these agreements, filing actions against

[3] "Bioequivalence" indicates that the rate and extent of absorption of the generic drug is not significantly different from that of the brand-name drug when administered at the same dosage.

[4] If the court grants a preliminary injunction before expiration of the 30-month period, then the ANDA will be approved on the date the court finds the patent invalid or not infringed.

[5] If the patent holder does not file suit, then the FDA may approve the ANDA immediately, provided all other requirements are met.

[6] The 30-month stay may be extended if the brand name company lists an additional relevant patent *after* the generic company filed its ANDA. In this instance, the generic company must re-certify with respect to the newly listed patent. If the brand name company files suit within 45 days of notification, an *additional* 30-month stay of ANDA approval will be generated from the date of notification.

Abbott/Geneva, and Hoechst Marion Roussel/Andrx. In addition, there have been several private actions filed by direct and indirect purchasers, including actions against these same parties.

While these agreements may harm short-term competition, as discussed below, they may also enable the branded company to more effectively protect its returns to innovation as provided for by its patent right, and may significantly reduce the cost and uncertainty of litigation, as is the case with settlements in general.

Per se v rule-of-reason treatment

Section 1 of the *Sherman Act* prohibits "[e]very contract, combination in the form of trust or otherwise, or conspiracy, in restraint of trade or commerce …." This prohibition has been interpreted by US courts to cover "unreasonable" contracts – ie those that harm competition. Consequently, some types of agreements have been viewed as, by their nature, inherently anticompetitive, with little potential for procompetitive benefits. These agreements, such as price fixing agreements and market allocation agreements, have been labeled "per se" violations of s 1 of the *Sherman Act*, that is, necessarily anticompetitive with little need for investigation of the facts surrounding the specific agreement.[7] However, other types of agreements, such as exclusive contracts and patent pools, are recognised to have both potentially anticompetitive and procompetitive aspects to them, and therefore are treated with a "rule of reason" analysis – whether they are anticompetitive is only determined after a thorough investigation of the facts surrounding a specific agreement.

In recent months, interim settlement agreements between branded and generic drug companies have received very different treatment in two different decisions by US Courts of Appeals. The Sixth Circuit ruled that these agreements are per se violations, while the Eleventh Circuit ruled that they should be treated under a rule of reason approach.

In re Cardizem CD Antitrust Litigation (Sixth Circuit)

Hoescht Marion Roussel (HMR) manufactures Cardizem CD, which is used to treat angina and hypertension and as a prevention for heart attacks and strokes. Andrx is a manufacturer of generic pharmaceuticals that filed a Paragraph IV certification ANDA with respect to HMR's patents on Cardizem CD.

In April 1998, HMR and Andrx entered an agreement whereby Andrx agreed not to market a generic form of Cardizem until the earlier of:

(1) a final judicial ruling declaring that the patent was invalid or not infringed;

(2) HMR entering a licence agreement with Andrx; or

(3) HMR entering a licence agreement with another generic manufacturer.

Andrx also agreed not to transfer its rights to the 180-day exclusivity period to another competitor. In exchange, HMR agreed to pay Andrx US$40 million per year.

A plaintiff class of direct purchasers filed suit against HMR and Ardrx, alleging that the agreement was a violation of s 1 of the *Sherman Act*. In 2000, the district court granted the plaintiffs' motion for partial summary judgment, ruling that the agreement constituted a restraint of trade that is per se illegal under s 1 of the *Sherman Act*.

In an April 2003 opinion, the Sixth Circuit upheld the finding of the district court stating:

> There is simply no escaping the conclusion that the [HMR-Andrx] Agreement, all of its other conditions notwithstanding, was, at its core, a horizontal agreement to eliminate competition in the market for Cardizem CD throughout the entire United States, a classic example of a per se illegal restraint of trade.[8]

[7] While it is possible that some of these agreements may in fact be procompetitive, for per se violations courts have felt that this possibility is so unlikely that it doesn't warrant the judicial resources a fact intensive investigation would require.

[8] *In re Cardizem Antitrust Litigation* 332 F 3d 896 at 908 (6th Cir 2003).

Valley Drug Co v Geneva Pharmaceuticals Inc (Eleventh Circuit 2003)

Abbott manufactures Hytrin, the branded version of terazosin hydrochloride (terazosin), which is used to treat hypertension and benign prostatic hyperplasia. Geneva is a manufacturer of generic pharmaceuticals that filed Paragraph IV certification ANDAs with respect to certain Abbott patents on terazosin.[9]

In April 1998, Abbott and Geneva entered an agreement whereby Geneva agreed not to sell a generic form of terazosin until the earlier of:

(1) the expiration of Abbott's patent;

(2) the introduction of generic terazosin by another competitor; or

(3) a final judicial ruling declaring that the patent was invalid or not infringed.[10]

Geneva also agreed not to transfer its rights to the 180-day exclusivity period to another competitor. In exchange, Abbott agreed to pay Geneva $4.5 million per month until entry by another generic manufacturer or the district court ruled that Abbott's patents were valid and infringed.

A plaintiff class of direct purchasers filed suit against Abbott and Geneva, alleging that the agreement was a violation of s 1 of the *Sherman Act*. In December 2000, the district court granted the plaintiffs' motion for summary judgment, that the agreements were per se illegal under s 1 of the *Sherman Act*.

In September 2003, the Court of Appeals for the Eleventh Circuit, in clear contrast to the Sixth Circuit decision discussed above, found that the district court had erred in treating the settlement agreements as per se violations of the *Sherman Act*.

> these [aspects of the patent settlement] are at the heart of the patent right and cannot trigger the per se label. Unlike some kinds of agreements that are per se illegal whether engaged in by patentees or anyone else, such as tying or price-fixing, the exclusion of infringing competition is the essence of the patent grant … Because the district court failed to consider the exclusionary power of Abbott's patent in its antitrust analysis, its rationale was flawed and its conclusion that these agreements constitute per se violations of the antitrust laws must be reversed.[11]

Discussion

The conflicting appellate court decisions in the *Cardizem* and *Valley Drug cases* highlight the difficult tradeoffs between protecting competition and protecting intellectual property rights.[12] Antitrust laws aim to protect consumers, who stand to benefit from significantly lower prices that often result from generic entry. However, patent laws aim to protect the patent holder's rights to monopoly rents during the life of the patent. Intellectual property rights provide incentives for continued innovation in pharmaceutical research and new product development, from which consumers stand to benefit in the long run.

Clearly a tradeoff exists if generic entry occurs before the patent litigation is resolved: higher consumer surplus in the short-run may be gained at the expense of reduced incentives for future innovation (which may lead to lower consumer surplus in the long run). Treatment of these settlement agreements as per se illegal may therefore reduce intellectual property protection unnecessarily (and as a result, innovation and the associated long-run benefits to consumers).

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[9] Geneva filed separate ANDAs for the capsule and tablet forms of terazosin. However, Abbott did not file suit within 45 days for infringement related to patents on the capsule form. Thus, no 30-month stay was imposed for that form of terazosin.

[10] Abbott entered a separate agreement with Zenith, another generic manufacturer. Zenith and Abbott reached a tentative settlement agreement, and therefore Zenith was not a party to the appeal (although the Eleventh Circuit applied a similar reasoning to the district court's treatment of the Abbott-Zenith Agreement).

[11] *Valley Drug Co v Geneva Pharmaceuticals Inc* 344 F 3d 1294 at 1306 (11th Cir 2003).

[12] In another significant opinion in recent months, the Federal Trade Commission (FTC) applied a rule-of-reason analysis in concluding that settlement agreements between Schering-Plough, Upsher-Smith and American Home Products were anticompetitive. The FTC's accompanying order imposed a relatively broad prohibition of settlement agreements of this type, making exceptions only where payments to the generic "are linked to litigation costs, up to $2 million, and that are notified to the commission." See www.ftc.gov/opa/2003/12/schering.htm viewed 27 May 2004.

A settlement agreement that delays entry of a generic drug and raises prices paid by consumers may be deemed anticompetitive, ex post, if the brand's monopoly is based on an invalid patent or one that is not infringed. Conversely, a settlement that preserves the brand's monopoly when the patent is valid and infringed protects the patent holders' intellectual property rights and the returns for innovation to which it is entitled. The problem, of course, is that there is often considerable uncertainty over whether the patent is valid and infringed.

Some observers have opined that a large payment from the brand to the generic (as in the case of the Cardizem and Hytrin cases) strongly suggests that the patent is "weak" – ie likely to be found invalid or not infringed. [13] Otherwise, they argue, the brand would not be willing to share the rents conveyed by the patent with the generic. But this logic assumes away such real world complications as litigation costs, bankruptcy, asymmetric information, and additional uncertainty. The size of the payment not only reflects the branded firm's expected probability of validity and infringement, but also its beliefs regarding the generic company's ability to pay any assessed damages and the probability of generic entry. To understand the potentially procompetitive aspects of a payment from the branded company to the generic company, it is useful to more carefully examine the factors that would be considered by both the branded and generic companies when deciding whether to enter a settlement agreement.

Generic entry typically lowers average drug prices significantly; [14] however, it generally does not have much effect on total demand for the drug. Consequently, the profits earned by the generic company may be much lower than those lost by the branded company. The generic company therefore faces the possibility that it could be held liable for large damages, if after its entry the patent is found to be valid and infringed.

While this risk may deter the generic entry, other factors also affect the generic firm's decision to enter *after* the 30-month stay expires, but *before* the patent litigation is resolved. Specifically, this decision also depends on the generic firm's expectations concerning the probability the patent will be found valid and infringed, its expected profits from entry, the amount of damages for which it may be held liable, and its ability to pay those damages. If the generic firm cannot afford to pay the potentially large damages award, the level of deterrence achieved is effectively truncated.

By comparison, the branded manufacturer has its own information and beliefs concerning the probability that its patent is valid and infringed. In addition, the branded manufacturer considers the probability that the generic will enter before the litigation is resolved, as well as the generic company's ability to compensate it for damages should the generic be found liable for infringement.

A large settlement payment could indicate the branded company's expectation that it would be significantly undercompensated if its patent were found to be valid and infringed. Because the generic will usually sell at a price substantially below the branded price (which is where the antitrust concerns stem from), the profits that the generic company will earn after entry are likely to be much smaller than the profits the branded company would have earned if the generic hadn't entered. Suppose the patent were to be found valid and infringed, months or years after generic entry. It is not clear that the generic producer would be able to pay the full amount of lost profits of the branded company, since these may be several times the actual profits that the generic producer had earned. Therefore, a large settlement payment from the branded producer to the generic producer may not be indicative of a "weak" patent, but merely the belief of the branded firm that it has a relatively low probability of recovering the full amount of its lost profits. [15]

A large payment could also indicate a significant difference in beliefs about the generic company's ability to enter the market upon FDA approval. For example, in the terazosin case, the defendants argued that, while Abbott believed Geneva would be able to enter upon FDA approval, Geneva was aware of manufacturing problems that would have delayed its entry. Therefore, Abbott was willing to pay to protect what it believed to be its valid monopoly rents, while Geneva was

[13] See, for example, Shapiro, n 1.

[14] While the price of the branded drug may, in some cases, increase after generic entry, the average price paid will decrease due to the significant penetration of generic drugs.

[15] For a more detailed model of this issue, see Langenfeld and Li, n 1.

willing to accept a payment that may have been less than the profits it would have obtained upon entry, to stay off the market.

There are several aspects of patent settlement agreements that may appear, on their face, to reduce competition, but may in fact be procompetitive if the patent were ultimately found valid and infringed. For example, some settlement agreements have provided for generic entry before the expiration of the patent. If the patent would have ultimately been found valid and infringed, then settlement could provide for generic entry at a date earlier than that which would have been achieved otherwise. Some patent settlement agreements lead to licensing of other products, thereby increasing competition in other markets. In addition, settlement agreements that provide payments to the generic company may help to make the generic a more viable competitor once patent does expire.

Finally, settlement of litigation is often a cost effective way of resolving patent disputes, which is why branded firms may be willing to pay to avoid the costs of litigation. To chill the use of these settlements by treating them as per se violations would increase the cost enforcing patent rights. The Eleventh Circuit recognised this additional incentive in their decision.[16]

While there certainly exists the potential for abuse of the provisions of Hatch-Waxman, there are a variety of circumstances in which a settlement involving payments from the branded company to the generic company is consistent with a patent that is valid and infringed. These settlements – which protect the incentives of branded drug companies to innovate – protect long run competition in the industry. Therefore, although these settlement agreements may warrant antitrust scrutiny, it seems clear that they should be treated under the rule of reason approach. The factors discussed above (eg the ability of the generic company to pay any damages, the ability of the generic company to enter the market upon FDA approval) provide judges with factors to consider when determining the competitive implications of an individual agreement.

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[16] *Valley Drug Co v Geneva Pharmacueticals Inc* 344 F 3d 1294 at 1306 (11th Cir 2003).