The legality of reverse payment settlements in Paragraph IV disputes

'Pay-for-delay' agreements between innovator and generic manufacturers have been the subject of much controversy. Several cases have raised questions over the legality of these payments

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Substantial controversy surrounds reverse payment settlements in pharmaceutical patent cases arising under the Drug Price Competition and Patent Term Restoration Act 1984 (the Hatch-Waxman Act).

The Hatch-Waxman Act allows a generic drug company to file an abbreviated new drug application (ANDA), permitting it to avoid time-consuming and expensive clinical studies and obtain Food and Drug Administration (FDA) approval by establishing "bioequivalence" to a previously approved brand-name drug product (21 USC Section 355(j)(2)(A)(iv)). If the branded product is covered by a patent, the generic company can choose to wait until the patent expires. However, the generic company often decides to challenge the patent – that is, the generic company certifies that the patent "is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted" (*id* at Section 355(j)(2)(A)(vii)(IV)). This certification is an act of patent infringement and the patent holder has 45 days from receiving notice of the certification to sue to protect its rights. Aside from legal fees, the generic patent challenger has little to lose in ensuing patent litigation. No actual damages for infringement can be awarded and such cases are not subject to a charge of wilful infringement (see *In re Tamoxifen Citrate Antitrust Litig*, 466 F3d 187, 206-07 (2d Cir 2006); *Glaxo Group Ltd v Apotex, Inc*, 376 F3d 1339, 1350-51 (Fed Cir 2004)). There is little to no recourse for a patent holder that is faced with a baseless certification (see *Yamanouchi Pharm Co v Danbury Pharmacal Inc*, 231 F3d 1339, 1346 (Fed Cir 2000), in which attorney's fees were awarded for baseless certification and pursuit of frivolous arguments during litigation). Further, as an incentive to file an ANDA, the act gives the first ANDA filer a 180-day exclusivity period during which the FDA cannot approve the ANDA of another generic manufacturer (see 21 USC Section 355(j)(5)(B)(iv)). During this exclusivity period, the first generic can take up to 80% of the branded product's sales.

Thus, in a Hatch-Waxman patent challenge, almost all of the risk falls on the branded company, which faces the possibility that it will lose nearly all of its market share and its patent protection. Given the uncertainty in any litigation and the high stakes for the branded company, a logical structure for a settlement would be a payment by the brand manufacturer to the generic and an agreement on a specific generic entry date, typically before the patent expiration but later than could have been realised had the patent challenge succeeded. However, such settlement structures have been criticised by the Federal Trade Commission (FTC) and the Department of Justice (DOJ) as potentially violating antitrust laws. In response to that criticism, the majority of circuit courts have adopted the rule that reverse payment settlements can pass antitrust scrutiny unless:

- The agreement exceeds the exclusionary scope of the patent.
- The patent was obtained by fraudulent

means.
- The underlying infringement lawsuit was objectively baseless.

This article discusses the major cases in this area and examines the current position of the FTC and DOJ on these issues.

***In re Cardizem CD Antitrust Litigation* – Sixth Circuit**

Only one circuit court decision has found antitrust liability resulting from a reverse payment settlement, although it was based on an unusual set of facts. The patent in suit claimed an extended-release formulation of diltiazem hydrochloride with up to 45% drug release within 18 hours of ingestion (*In re Cardizem CD Antitrust Litig*, 332 F3d 896, 902 (6th Cir 2003)). The generic challenger denied infringement, stating that the release of the drug from its product was not less than 55% over 18 hours (*id*). In an interim settlement, the generic agreed to stay off the market for a period of time in exchange for US$10 million per quarter, or US$40 million per year (*id* at 902-03). By the time the agreement was terminated, the generic had received more than US$89 million from the brand manufacturer (*id* at 903). Direct and indirect drug purchasers challenged the agreement under federal and state antitrust law (*id* at 900).

The Sixth Circuit found that the agreement was *per se* illegal, despite the existence of the patent. According to the court, the agreement operated as a horizontal restraint on competition, which guaranteed the brand manufacturer that its only potential competitor would refrain from marketing its generic product even after it received FDA approval and likewise delayed the entry of other competitors, which were barred until the expiration of the 180-day exclusivity period (*id* at 907-08).

***Valley Drug Co v Geneva Pharms, Inc* – Eleventh Circuit**

In *Valley Drug*, the patent holder entered into agreements with two generic manufacturers whereby the generics would refrain from marketing generic terazosin hydrochloride in exchange for quarterly payments of US$6 million to one generic and monthly payments of US$4.5 million to the other (*Valley Drug Co v Geneva Pharms, Inc*, 344 F3d 1294, 1300 (11th Cir 2003)). The patent was subsequently found invalid (*id* at 1301). Private plaintiffs brought an antitrust lawsuit alleging that the agreements were *per se* illegal under Section 1 of the Sherman Act and the district court agreed.

The Eleventh Circuit reversed, finding *per se* treatment inappropriate because of the existence of the patent at the time that the agreement was made (*id* at 1304). The court found that the agreement did not exceed the potential exclusionary effect of the patent, regardless of the later holding that the patent was invalid (*id* at 1311 and n 27). Because the agreement contemplated generic entry into the market prior to patent expiration, the court found that the agreement was narrower than the patent's exclusionary effect (*id* at 1305). However, the court noted that antitrust liability can attach in circumstances where evidence exists of fraud against the US Patent and Trademark Office or sham litigation (*id* at 1309 and n 21).

***Schering-Plough Corp v FTC* – Eleventh Circuit**

Schering owned a formulation patent on the extended-release coating of its K-Dur 20® potassium supplement (*Schering-Plough Corp v FTC*, 402 F3d 1056, 1058 (11th Cir 2005)). In settlement, Schering and generic challengers agreed that in exchange for payments reaching US$60 million, the generics would remain off the market for a specified period of time and Schering would obtain licences on unrelated products owned by the generics (*id* at 1059-61).

Following an administrative proceeding, the FTC determined that the agreement would injure competition and consumers, and articulated a ban on settlements where the generic drug manufacturer received anything of value to defer its activities. However, the FTC ruled that "if payments can be linked to litigation costs (not to exceed $2 million), and the Commission is notified of the settlement, then the parties need not worry about a later antitrust attack" (*id* at 1062).

The Eleventh Circuit reversed the FTC's determination and found that because of Schering's underlying patent right, the agreements did not result in any "unreasonable" restraint of trade. The court found the agreements sufficiently narrow because they were commensurate with the protections under the patent, employing language identical to the patent (*id* at 1073, 1076).

***In re Tamoxifen Citrate Antitrust Litigation* – Second Circuit**

This case involved Barr Laboratories' desire to market a generic form of Zeneca Inc's successful breast cancer drug tamoxifen (*In re Tamoxifen Citrate Antitrust Litig*, 466 F3d 187 (2d Cir 2006)). The parties settled the case during an appeal of the district court's finding that the patent covering tamoxifen

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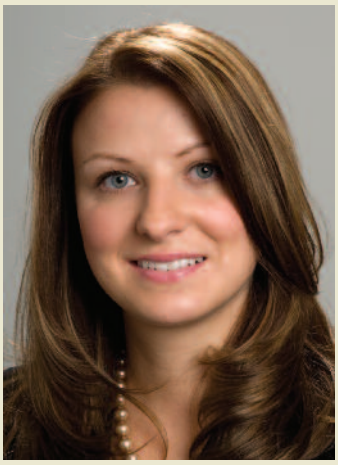

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was invalid and unenforceable (*id* at 193). In exchange for US$21 million and a licence to sell Zeneca-manufactured tamoxifen in the United States, Barr agreed to refrain from marketing its own tamoxifen product until the patent expired (*id* at 193-94).

Consumer groups filed antitrust actions, alleging that the settlement agreement unlawfully permitted Zeneca to resuscitate a patent that was invalid and unenforceable and to continue to monopolise the market without competition (*id* at 196-97). The Second Circuit affirmed dismissal of the case, explaining that the agreement did not exceed the scope of the patent because it did not prevent the introduction of non-infringing products, as was the case in *Cardizem CD*. In particular, the court noted that the agreement could not possibly reach beyond the patent to non-infringing products because a compound patent (as opposed to a formulation patent) "by its nature, excludes all generic versions of the drug" (*id* at 214).

Arguing that a more searching scrutiny was warranted, Judge Pooler dissented from the standard adopted by the majority. Under her proposed approach, the reviewing court should consider:

- The strength of the patent as it appeared at the time of the agreement and the amount that the patent holder paid to keep the generic manufacturer from marketing its product.
- The amount that the generic manufacturer stood to earn during its period of exclusivity.
- Any ancillary anti-competitive effects of the agreement (*id* at 228 (Pooler, J, dissenting)).

***In re Ciprofloxacin Hydrochloride Antitrust Litigation* – Second Circuit and Federal Circuit**

The Second Circuit tacitly affirmed its holding in *Tamoxifen* in *Ark Carpenters Health and Welfare Fund v Bayer AG*, 604 F3d 98 (2d Cir 2010). Bayer was the owner of a compound patent covering ciprofloxacin hydrochloride, the active ingredient in its popular antibiotic Cipro® (*In re Ciprofloxacin Hydrochloride Antitrust Litig*, 363 F Supp 2d 514, 518 (ED NY 2005)). Shortly before the trial was set to begin, Bayer and the generic challengers entered into settlement and supply agreements (*id* at 519). The settlement agreement with generic challenger Barr Laboratories, Inc provided that in exchange for US$49.1 million, Barr would amend its ANDA filing and market generic ciprofloxacin only after expiration of the patent (*id*). Under the supply agreement, Barr agreed not to manufacture or have manufactured a generic form of Cipro® in the United States in exchange for additional quarterly payments or a supply of Cipro® from Bayer (*id*). By the time the patent expired in December 2003, Bayer had paid Barr approximately US$398 million (*id*).

Two classes of plaintiffs, direct purchasers and indirect purchasers, filed antitrust claims against the parties. The district court found that the agreements were not unlawful because they fell within the scope of the patent (*id* at 520). The district court aligned itself with the Second Circuit majority view that an independent analysis of the validity of the patent was improper in determining the reasonableness of a settlement agreement (*id* at 530).

The indirect purchasers' appeal was heard by the Federal Circuit and the direct purchasers' appeal was heard by the Second Circuit. The Federal Circuit agreed that because a patent by its very nature is anti-competitive, any anti-competitive effects within the scope of the patent could not be redressed by antitrust law (*In re Ciprofloxacin Hydrochloride Antitrust Litig*, 544 F3d 1323, 1333 (Fed Cir 2008)).

The Second Circuit found that it was bound by the standard adopted in *Tamoxifen*, finding that the agreement did not exceed the exclusionary scope of the patent where "(1) there was no restriction on marketing non-infringing products; (2) a generic version of the branded drug would necessarily infringe the branded firm's patent; and (3) the agreement did not bar other generic manufacturers from challenging the patent" (*Ark Carpenters Health and Welfare Fund v Bayer AG*, 604 F3d 98, 106 (2d Cir 2010)). Further, there was no allegation of fraud or sham litigation (*id*). *En banc* rehearing was denied (*Ark Carpenters Health and Welfare Fund v Bayer AG*, 625 F3d 779, 781 (2d Cir 2010)).

***In re K-Dur Antitrust Litigation* – pending before the Third Circuit**

This class action, brought on behalf of direct purchasers of K-Dur 20®, arose from the same agreement considered by the Eleventh Circuit in *Schering-Plough Corp v FTC*.

The special master presiding at the district court level employed the framework used by the Second, Eleventh and Federal Circuits and found that the settlement agreements were not unlawful (*In re K-Dur Antitrust Litig*, No 01-1652, 2009 WL 508869 at 27-31 (D NJ Feb 6 2009)). The antitrust plaintiffs appealed to the Third Circuit and argument was heard on 12th December 2011.

The FTC and the DOJ filed amicus briefs

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to the Third Circuit, arguing in favour of a "truncated rule of reason" analysis. Under the analysis proposed by the DOJ, the plaintiff can establish a *prima facie* antitrust violation by showing first that there was in fact a reverse payment (Brief for the United States as Amicus Curiae, at 24-25; available at www.justice.gov/atr/cases/f271300/271395.pdf). The burden then shifts to the defendants either to negate the *prima facie* case by showing that the payment was actually for some legitimate activity (eg, "back-up manufacturing") or to rebut the *prima facie* case by providing a reasonable explanation of the payment (*id* at 28-29 and n 13).

Notably, the DOJ stated that there is no violation where the payment is commensurate with the patent holder's avoided litigation costs (*id* at 29). This calculus can include the cost of business disruption as well as a "modest" payment to "bridge the gap" between the parties' expectations of the outcome of litigation (*id* at 29-30). However, where the payment exceeds the avoided costs of litigation, a court should look at the amount of competition provided for in the agreement. The DOJ argued that if no competition is contemplated until the expiration of the patent, the agreement should be deemed unlawful; but if the settlement allows for generic competition before patent expiration, the agreement is lawful if it is consistent with the parties' "contemporaneous evaluations" of the outcome of the litigation (*id* at 30 -31).

In its amicus brief, the FTC similarly argued for a flexible rule of reason analysis. According to the FTC, where any substantial payment forestalls competition, a presumption of illegality is justified and the burden then shifts to the settling parties to justify the agreement (Brief of the Federal Trade Commission as Amicus Curiae, a t 13, 22-25; available at www.ftc.gov/os/2011/05/110518amicusbrief.pdf).

No decision had been reached in the case as of the date of writing.

Other recent statements

FTC Commissioner Rosch recently stated that in the absence of judicial or legislative intervention regarding reverse payment settlements, the FTC may yet regulate Hatch-Waxman settlements by enacting agency rules (Rosch, *Antitrust Evaluation,* at *8-9 available at 2011 WL 6140878). He has suggested that such rules would not ban pay-for-delay agreements outright, but would treat them as "inherently suspect" (*id* at 9).

Further, the FTC continues to monitor agreements filed pursuant to the Medicare Prescription Drug, Improvement, and Modernisation Act 2003. The FTC found that in 2011 "28 final settlements contained both compensation to the generic manufacturer and a restriction on the generic manufacturer's ability to market its product" (Agreements Filed With the Federal Trade Commission Under the MMA: Overview of Agreements Filed in FY 2011 (Oct 2011); available at www.ftc.gov/os/2011/10/1110mmaagree.pdf). The FTC staff analyses each agreement to determine whether an enforcement action is warranted (Rosch, *Antitrust Evaluation,* at 10).

Although the courts have largely refused to proscribe substantial reverse-payment settlements, regulatory agencies continue to monitor such settlements and litigants must be mindful that any payment beyond reasonable avoided litigation costs will be subject to close scrutiny. ■

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