

# INTELLECTUAL PROPERTY

## Third party without remedy in Orange Book case

4th Circuit holds that FDA's refusal to list a patent was not arbitrary or capricious.

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SPECIAL TO THE NATIONAL LAW JOURNAL

"I'VE GOT A LITTLE list...of patents that won't be missed."

The lord high executioner in Gilbert & Sullivan's Mikado had a list of people that wouldn't be missed. The list referred to above is the list of patents in the Food and Drug Administration's Approved Drug Products, commonly called the Orange Book. Listing in the Orange Book vastly increases the strength of a patent—the ability of the patent to preclude generic competition to an FDA-approved

drug product. Conversely, keeping a patent off the Orange Book List can accelerate generic competition. The case of *aaiPharma v. Thompson*, 2002 WL 1473429 (4th Cir. July 10, 2002), concerns whose patents can be listed in the Orange Book, and, therefore, how many patents will be listed.

Before the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act (P.L. 98-417, codified at 21 U.S.C. 355(b) and (j) and 35 U.S.C. 271(e) and 156), the Orange Book was a list of FDA-approved drugs. The Hatch-Waxman Act required the applicant for a new drug application (NDA) to submit a list of "of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 35 U.S.C. 355(b)(1).

To market a generic version of the approved drug, the Hatch-Waxman act allows the filing of an abbreviated new drug application (ANDA), which does not need to show the safety and efficacy of the drug, but which can refer to the safety and efficacy studies which were already submitted for the approved drug

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product. The ANDA, however, must contain a certification with respect to the patents listed in the Orange Book. A "paragraph IV certification" certifies that the listed patent(s) is invalid, unenforceable or would not be infringed by the ANDA product. 21 U.S.C. 355(j)(2)(A)(vii).

An applicant that files a paragraph IV certification must notify the holder of the NDA and the owner of the listed patent of the paragraph IV certification and must supply a detailed statement of the factual and legal bases

for the ANDA applicant's opinion that the patent(s) are invalid, unenforceable or not infringed. 21 U.S.C. 355(j)(2)(B) The act of certifying is a technical act of patent infringement. 35 U.S.C. 271(e)(2). The patent owner can sue for patent infringement on the basis of that technical act of infringement at any time.

But if the patent owner brings a patent-infringement action within 45 days of receipt of the notice, the FDA is forbidden to approve the ANDA for 30 months. 21 U.S.C. 355(j)(5)(B)(iii). The FDA can approve the ANDA earlier if there is a final decision of a court in favor of the ANDA applicant, holding the patent invalid, unenforceable or not infringed, and the court in which the patent litigation is taking place may shorten (or lengthen) the 30-month period for failure to expedite the action.

### The 30-month period

The sole reason for the elaborate regulatory scheme of patent listing, certification and notice is to allow the owner of the approved drug and the ANDA applicant time to litigate the patent before the ANDA applicant begins marketing the generic drug. The NDA holder/patentee wants to delay generic competition as long as possible, and certainly at least until there is a decision by a court that there are no patent barriers; the ANDA applicant wants to be sure that it will not be liable for potentially ruinous damages. However, the 30-month period can be an end in itself. Most patents prevent competition only to the extent that potential infringers value their strength.

But listed patents, whether strong or weak, result in the same 30-month period of market exclusivity.

The statute requires the NDA holder to list "any" appropriate patent, and for many products, multiple patents are listed, each of which potentially carries its own 30-month period. Although an applicant can certify against all listed patents when the ANDA is filed, it cannot certify against patents which are not listed, and it must certify against each new patent that is added to the Orange Book. Thus, an NDA holder could potentially delay generic competition indefinitely by listing a new patent every couple of years, each one starting a new 30-month period.

The Federal Trade Commission (FTC) recently found that patents added to the Orange Book after an ANDA had already been filed resulted in additional litigation, which delayed generic entry into the market for between four and 40 months after the initial 30-month period, but that in every case that was not settled, the subsequently listed patents were found invalid or not infringed. "Generic Drug Entry Prior to Patent Expiration: An FTC Study," available at [www.ftc.gov/opa/2002/07/genericdrugstudy.htm](http://www.ftc.gov/opa/2002/07/genericdrugstudy.htm).

### Whose patent gets listed?

*aaiPharma v. Thompson*, a case of first impression, concerned an attempt by a party other than the owner of an NDA to list a patent in the Orange Book for that NDA. Lilly had already listed several patents for Prozac, leading to protracted litigation in which Lilly's last remaining patent was held invalid, opening the door to generic competition on Aug. 2, 2001. *Eli Lilly & Co. v. Barr Laboratories Inc.*, 251 F.3d 955, 962 (Fed. Cir. 2001). *aaiPharma*, a company unrelated to Lilly, obtained a patent (the '853 patent) relating to fluoxetine, the active ingredient in Prozac, on July 10, 2001, weeks before several generic manufacturers were set to begin marketing.

*aaiPharma* first approached Lilly, suggesting that Lilly take a license under the *aaiPharma* patent and list the patent in the Orange Book. When Lilly refused, *aaiPharma* requested the FDA to list the patent. Following its

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regulations, the FDA refused, and aaiPharma brought this suit against the FDA to force the FDA to list aaiPharma's patent.

The 4th U.S. Circuit Court of Appeals affirmed the trial court, holding that although aaiPharma had a right to have its patent listed in the Orange Book, the FDA's refusal to list it was not arbitrary and capricious nor otherwise not in accordance with law, and therefore, aaiPharma was without remedy to force the FDA to list its patent.

The 4th Circuit conclusorily disposed of the first point, that aaiPharma had a right to have its patent listed in the Orange Book, simply quoting the statute, and concluded that "if [as aaiPharma asserts] the '853 patent claims Prozac in the sense provided in § 355(c)(2), Lilly is obligated to submit the '853 patent for listing in the Orange Book and the FDA is required to publish the submitted listing." The statute provides: "The NDA holder shall file with the [FDA] the patent number and the expiration date of any patent which claims the drug for which the application was submitted....Upon the submission of patent information under this subsection, the [FDA] shall publish it." 21 C.F.R. 355(c)(2)).

The rest of the 4th Circuit's opinion explains why aaiPharma has a right without a remedy. First, aaiPharma had no means to compel Lilly to list the '853 patent, because there is no private right of action against an NDA holder to force the NDA holder to list (or delist) a patent. *Andrx Pharm. Inc v. Biovail Corp.*, 276 F.3d 1368, 1373-74 (Fed. Cir. 2002). Second, the FDA's refusal to list the patent was in accord with its duly issued regulations, which were within its discretion.

### Purely ministerial role

The FDA has taken the position that it does not have the resources to police the Orange Book, nor the necessary expertise in patent matters to do so. 59 Fed. Reg. 50,338, 50,345 (Oct. 3, 1994). Therefore, it exercises a purely ministerial role over Orange Book listings. If questions regarding patent listings are brought to the FDA's attention, the FDA will request the NDA holder to confirm the accuracy and relevance of the listings. Unless the NDA holder withdraws or amends the patent information in response to the FDA's request, the FDA will not change the patent listing. 21 C.F.R. 314.53(f). "In short, the FDA's position is that if the NDA holder stands on its Orange Book listing, aggrieved parties are out of luck." *aaiPharma v. Thompson*, 2002 WL 1473429, at \*7.

The 4th Circuit, however, agreed that the

FDA's position was a permissible interpretation of the statute. Although the Hatch-Waxman Act could be interpreted as requiring the FDA to ensure the accuracy and relevance of Orange Book listings, "on the better reading...the FDA is required only to ensure that each NDA applicant has submitted either a list of patents claiming its drug or a declaration that there are no patents to be listed." *Id.* at \*9. Because the FDA had discretion about whether to take on enforcement responsibilities for policing the Orange Book, the FDA's rationale for adopting its ministerial-role-only policy—that it lacked resources or expertise—was sufficient to satisfy the requirement of reasoned agency decision-making. *Id.* at \*12.

Although the FDA's refusal to take more than a ministerial role left aaiPharma without a remedy, the court could "not accept the proposition that

an agency's failure to fill an enforcement gap created by statute is necessarily arbitrary and capricious." *Id.* at \*13.

However, the court expressed its sympathy that aaiPharma was left without a remedy but concluded that "until Congress takes further action to address the enforcement gap in Hatch-Waxman's patent listing provision, the [FDA] may persist in its purely ministerial approach to the Orange Book listing process." *Id.*

The 4th Circuit's decision preserved the status quo: The FDA need not list third-party patents—unless submitted by the NDA holder.

The status quo, for obvious reasons, is supported by the generic industry. Third-party patents that are not sponsored by the NDA holder will usually result in the listing of multiple patents, which tends to delay introduction of generic drugs, since later-listed patents tend to be weak—either invalid or not infringed by the generic products. See "Generic Drug Entry Prior to Patent Expiration: An FTC Study," *supra*, at n.11.

ANDA applicants, if they were able, would likely take the risk and market in the face of these later-issued patents—if they were not delayed by the 30-month period. Brand-name companies, too, have reason to support the status quo. Third-party patents can lead to allegations of antitrust violations against the brand-name company. See Gardiner Harris, "Companies: Bristol-Myers Is sued by 29 States Over Efforts to Block Generic Taxol," *Wall St. J.*, June 5, 2002, 2002 WL-WSJE 22214681. Such patents could, in certain circumstances, actually decrease the exclusivity enjoyed by the brand-name company.

The 4th Circuit opinion, however, suggests that the status quo is in real danger. The FDA's refusal to list aaiPharma's patent is not arbitrary and capricious only because the FDA exercises only a ministerial role with respect to the Orange Book patent listings. If, however, the FDA began to exercise a substantive role with respect to Orange Book listings, the FDA would have no basis to refuse to evaluate whether aaiPharma's patent should be listed.

Recently, amendments to the Hatch-Waxman Act have been proposed that would require the FDA to exercise more than a ministerial role. S.2677, introduced by Senator John D. Rockefeller, D-W.Va., this past June, would require the FDA to publish only "qualified" patent information in the Orange Book, that is, information which in fact relates to a patent, namely, patent information that meets the requirements of the statute. S.2677 § 205(b)(2), amending 21 U.S.C. 355(b)(1).

### The Rockefeller bill

Under the Rockefeller bill, therefore, the FDA would have more than a ministerial role in policing Orange Book listings. In that case, the FDA would have no basis to deny aaiPharma a substantive review of the appropriateness of a refusal to list the aaiPharma patent.

Fortunately, the Rockefeller bill provides a solution to the problem it creates. Under the Rockefeller bill, there can be only one 30-month period with respect to any ANDA. S.2677 section 206, amending 21 U.S.C. 355(j)((5)(B)(iii)). A similar provision is found in S.812, the McCain-Schumer bill, which was approved by the Senate on July 31, but which has not been signed into law. Without the incentive of the 30-month period, there would often be no reason for third parties such as aaiPharma to submit their patents for listing.

The FDA has recently promulgated regulations ([www.accessdata.fda.gov/scripts/oc/ohrms/advisdisplay.cfm](http://www.accessdata.fda.gov/scripts/oc/ohrms/advisdisplay.cfm), Oct. 24, 2002) under which only one 30-month period will be available per ANDA. The proposed rule will not be effective as to drugs for which ANDAs have already been filed.

The opportunity for mischief would still arise, however, when there are no patents listed by the brand-name company; when there are patents listed by the brand-name company, but no ANDAs have been filed at the time that the third party requests listing; and when any ANDA is filed after a third-party patent is listed. To ensure the preservation of the status quo, the Hatch-Waxman Act could be amended to provide explicitly that only NDA holders have the right to submit patents for listing in the Orange Book.

## aaiPharma was left without a remedy.