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Brief Analysis of Recent Pharmaceutical/IP Decisions

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AMERICAN BIOSCIENCE, INC. V. THOMPSON 269 F.3D1077, 2001 WL 1355189 (D.C. CIR. 2001)

On November 6, 2001, the U.S. Court of Appeals for the D.C. Circuit reversed a district court decision upholding the FDA's approval of Baker Norton Pharmaceutical's application for a generic version of the cancer treatment Taxol (paclitaxel). The Court ruled that the FDA's decision was arbitrary and capricious and remanded the case to the FDA for further proceedings.[1]

Background

This decision represents the near-culmination of a lengthy and procedurally convoluted lawsuit. In 1992, the FDA approved Bristol-Myers's New Drug Application (NDA) to manufacture paclitaxel, an anticancer drug. Five years later, Baker Norton submitted an Abbreviated New Drug Application (ANDA) for a generic version of Taxol. Bristol promptly initiated patent infringement proceedings against Baker Norton, thereby triggering a 30-month stay of approval of Baker Norton's ANDA, as dictated by the Hatch-Waxman Act. The 30-month stay expired in June 2000. For reasons that are unclear, the FDA did not approve Baker Norton's ANDA upon expiration of the stay.

Under 21 U.S.C. § 355(c)(2) of the Hatch-Waxman Act, if a relevant patent is issued after an NDA is approved, the NDA holder has 30 days from the date the patent was issued to "list" the patent. On August 1, 2000, American Bioscience received a patent ("the '331 patent") for a process that purported to deliver safer and more effective doses of paclitaxel. Ten days later, American Bioscience sued Bristol in the Central District of California for a TRO that would compel Bristol to submit the '331 patent for listing in the Orange Book. On August 11, 2000, the district court granted American Bioscience's request for a TRO and ordered Bristol to "immediately take all steps under its control to cause the FDA to list in its 'Orange Book' [American Bioscience's] Taxol Patent." Bristol complied with the TRO that same day. According to American Bioscience, Bristol's compliance with the TRO constituted a "listing" of the '331 patent within the meaning of 21 U.S.C. § 355(c)(2).

Several weeks later, the same court dissolved the TRO on the grounds that the Federal Food, Drug and Cosmetic Act did not provide American Bioscience with a private right of action to have its patent listed (a conclusion similar to that of the Federal Circuit in the BuSpar case, discussed below). The court ordered Bristol to "restore the status quo . . . [and] use its best efforts to cause the delisting of [American Bioscience's] '331 patent from the Orange Book." The court also recommended that the FDA toll the amount of time the TRO was in place.

Meanwhile, on August 14, 2000, Baker Norton filed a Paragraph IV certification for the '331 patent but neglected to notify Bristol and American Bioscience of the certification, as required by the Hatch-Waxman Act.[2] Two weeks later, the FDA tentatively approved Baker Norton's ANDA, subject to

[1] The factual background of this case is based on the D.C. Circuit opinion at 269 F.3d 1077, 1080–1081 (2001)

[2] When an applicant files an ANDA for a generic version of a drug listed in the Orange Book, the applicant must certify that any patent information listed in the Orange Book does not bar FDA approval of the generic version. One certification option, known as a Paragraph IV certification, states that the patent is invalid or will not be infringed by the manufacture, use or sale of the drug for which the ANDA applicant seeks approval. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

resolution of the '331 patent issues. On September 7, 2000, American Bioscience sued Baker Norton for patent infringement, but the FDA did not grant a stay. On September 11, 2000, Bristol informed the FDA that it was listing the '331 patent pursuant to the voluntary listing provision. According to the FDA, the September 11 letter amounted to a "late listing" of the '331 patent. *See American Bioscience, Inc. v. Shalala*, 142 F. Supp. 2d 1, 6 (D.D.C. 2000).

Three days later, on September 14, 2000, in a move that would become a major focus of controversy, Bristol informed that FDA that it was now de-listing the '331 patent to the extent it was listed pursuant to the California court's TRO, but that it did not mean to affect the "continued and continuous listing of the patent." That same day, Baker Norton withdrew its Paragraph IV certification. The following day, the FDA approved Baker Norton's ANDA without mentioning the '331 patent.

American Bioscience then sued in the U.S. District Court for the District of Columbia, claiming that the FDA violated the Administrative Procedure Act. The district court held, among other things, that the FDA acted properly in determining that Bristol did not list the '331 within the required 30 days.

On appeal, American Bioscience argued that the FDA acted contrary to law by approving Baker Norton's application in light of Bristol's listing of the '331 patent and that it was arbitrary and capricious for the agency to have concluded that Bristol's September 14 letter revoked the August 11 listing.

Discussion

The Court began its analysis of the merits by noting that the FDA's role in administering the Orange Book is purely "ministerial." That is, in listing patents in the Orange Book, the FDA simply follows the intent of the NDA holder. In this case, however, the Court found that the FDA had overstepped its ministerial role by relying on its reading of the district court order—to which the FDA was not a party—to trump Bristol's stated intent. Specifically, the D.C. Circuit found that the FDA ignored Bristol's intention, as stated in Bristol's September 14 letter, that the de-listing of the '331 patent pursuant to the California district court's order "not affect the continued and continuous listing of the patent. . . . "

According to the D.C. Circuit, the FDA "implicitly suggests" that Bristol's stated intent was "somehow inconsistent" with the California court's order, "and on appeal the government boldly contends that that intent—to continue its listing on a voluntary basis—is unacceptable without explaining why that should be so."[3] The FDA's reading of Bristol's letter thus was "unreasonable" and, in any event, was not entitled to any deference by the court. Indeed, the Court explained that "it is not at all clear to us that the FDA, under its regulations, would be authorized to reject the obvious intent of an NDA holder even if it acted directly contrary to a court order. Certainly, the FDA points us to no authority upon which it could rely to do so."[4]

The D.C. Circuit also dismissed suggestions that some of the parties to the case were engaged in certain underhanded machinations: Baker Norton "would have us believe that appellant and Bristol-Myers are in cahoots, that the California lawsuit was a Kabuki play and that they have a common objective to frustrate the introduction of generic versions of Taxol. The difficulty with these assertions—besides being not proven—is that the FDA . . . did not rely on this rationale. Nor is it clear that the FDA, as opposed to a district court in an antitrust or patent infringement case, could adjudicate such a claim." The Court thus declined to give any weight to Baker Norton's allegations or to concerns of the FTC and the public about "'the aggressive use of patent listings to delay generic competition.'"

On an earlier appeal in this case, the D.C. Circuit directed the district court to remand the case to the FDA to compile an administrative record, "consistent with our practice of remanding without vacating when we are unsure of the grounds the agency asserts to defend its action" (*American Bioscience v. Thompson*, 243 F.3d 579, 582–83 (D.C. Cir. 2001)). Now, on this second appeal, the Court determined that "the only appropriate course is to vacate the FDA's approval of [Baker Norton's] ANDA" and remand to the agency. Like the Federal Circuit in the BuSpar case (see below), however, the Court vacated without any further mandate. Indeed, the Court admitted that "[w]e frankly do not know what recourse is left to the FDA or other government agencies to take any steps that would affect the marketing of generic versions of Taxol. But we are convinced that the FDA's order, in this case, was arbitrary and capricious and must be vacated."

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[3] 269 F.3d at 1085
[4] Id.

MYLAN PHARMACEUTICALS V. THOMPSON, 268 F.3D 1323 (FED. CIR. 2001)

On October 12, 2001, the U.S. Court of Appeals for the Federal Circuit reversed a district court ruling requiring Bristol-Myers Squibb to delist a patent on buspirone hydrochloride from the FDA's Orange Book and directing the FDA to grant final approval of Mylan's generic buspirone product. The CAFC determined that neither the patent laws nor the Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act (FFDCA) allowed the district court to grant Mylan this declaratory relief. The CAFC did not reach the district court's holding that Bristol had improperly submitted its patent to the FDA for listing in the Orange Book.[5]

Background

The story behind this case begins in 1980, when Bristol obtained a patent covering the administration of buspirone to treat anxiety disorders. Six years later, the FDA listed Bristol's patent in the Orange Book as covering Bristol's FDA-approved drug BuSpar. Bristol's patent was set to expire on November 22, 2000, ending almost 15 years of exclusivity. In anticipation of the patent's expiration, Mylan and other generic makers had filed ANDAs and received tentative approvals for their generic buspirone products.

About 12 hours before Bristol's patent was set to expire, the U.S. Patent and Trademark Office issued patent 6,150,365 to Bristol, which Bristol immediately delivered to the FDA for listing in the Orange Book. The '365 patent contained one claim, directed toward a metabolite of buspirone, which Bristol sought to have listed in the Orange Book as covering buspirone. As a result of Bristol's 11th-hour listing, the FDA suspended approval of Mylan's ANDA and other ANDAs filed by prospective generic buspirone manufacturers.

Mylan then sued both the FDA and Bristol in the U.S. District Court for the District of Columbia. In March 2001, the district court held that under the Declaratory Judgment Act, Mylan was entitled to a declaration that the '365 patent was improperly listed in the Orange Book, as a defense to the infringement suit Bristol could have brought against Mylan under 35 U.S.C. § 271(e)(2).

The court then proceeded to construe '365 patent's claim and found that the patent did not claim the drug for which Bristol had submitted the application or a method of using such drug. As a result of the district court's ruling, Mylan and other generic makers received final approval of their ANDAs and began marketing their generic buspirone products.

Bristol immediately sought an interlocutory appeal of the district court's order. The FDA, which had opposed Mylan's position at the district court level, changed course on appeal and argued that Mylan had a cognizable cause of action against Bristol for declaratory judgment under the patent laws and that the FFDCA did not prohibit such a cause of action. By contrast, Bristol argued that Mylan's claim to delist a patent from the Orange Book was an impermissible attempt by a private party to enforce the FFDCA and that the district court should not have granted declaratory relief, because under the well-pleaded complaint rule, Bristol would have no cause of action against Mylan to "list" the '365 patent.

Discussion

Addressing only whether Mylan's cause of action arose under the patent laws as a defense to patent infringement, the CAFC framed the issue as one of first impression. The Court explained that because the Declaratory Judgment Act is remedial, "a party's legal interest under the Act must relate to an 'actual claim arising under federal law which another asserts against him.'" Under the "well-pleaded complaint rule," the court does not look to the plaintiff's complaint to determine which federal law is the basis of the declaratory plaintiff's cause of action, "but to the action that the declaratory defendant would have brought" to enforce its rights. Mylan argued that Bristol, the declaratory judgment defendant, would have brought an action for patent infringement under 35 U.S.C. § 271(e)(2). As Mylan explained, had it filed an ANDA with a Paragraph IV certification, Bristol would have charged it with infringing the '365 patent. One of the defenses to this infringement action would have been that Mylan was not required to file a Paragraph IV certification in the first place because Bristol had improperly listed the '365 patent in the Orange Book. The CAFC rejected this argument, holding that Mylan's defense was not a recognized defense to patent infringement.[6]

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[5] The facts here are drawn from the Federal Circuit's opinion at 268 F.3d 1323 at 1327.

[6] Id. at 1331.

The Federal Circuit also considered whether the Hatch-Waxman Act supplies a defense to patent infringement. Finding "no explicit provisions allowing an accused infringer to defend against infringement by challenging the propriety of the Orange Book listing of the patent," the Court concluded that Mylan's action was, in essence, an attempt to assert a private right of action for "delisting" under the FFDCA. And because the Hatch-Waxman Act did not modify the FFDCA's prohibition on private rights of action, the Court held that Mylan's claim was impermissible.[7]

Interestingly, the Court did not specifically order the FDA to remove the new BuSpar patents from the Orange Book or Mylan to stop selling its generic version on the market.

ANDRX PHARMACEUTICALS, INC., V. BIOVAIL CORPORATION, 256 F.3D 799 (D.C. CIR. 2001)

Andrx v. Biovail is a private antitrust suit by Biovail challenging the Andrx-Hoechst diltiazem (Cardizem) drug settlement. At issue was whether Biovail's suit against Andrx was properly dismissed on standing grounds. The district court had dismissed the claim with prejudice. The appellate court affirmed the dismissal but reversed the decision to dismiss with prejudice. Although a standing decision may not seem particularly noteworthy, the case may provide guidance to the Sixth and Eleventh Circuits as they consider the appeals of the Cardizem and Hytrin (terazosin) consumer treble damage suits.

The facts underlying the litigation and the agreement between Hoechst and Andrx are well known and are the subject of private consumer litigation and an FTC enforcement action.[8] Biovail was the next generic in line to receive FDA approval to market generic diltiazem. Andrx entered with its generic version of diltiazem in June 1999, and Biovail received final approval for its version in December 1999.

Standing litigation focuses on several issues: (1) whether the plaintiff has suffered injury in fact and whether the defendant's conduct caused the injury; (2) whether the injury is the type the antitrust laws were meant to prevent; (3) whether the harm was speculative; (4) whether there is a more appropriate plaintiff; and (5) whether there is a risk of duplicate recovery.[9] The court focused on the first two issues.

Injury in Fact and Causation

The district court had held that Biovail not only failed to plead an injury or a threatened injury but was unable to do so because Biovail had yet to receive FDA approval for its generic version of diltiazem and gave no assurance that it would have entered the market had it gained approval. The CAFC rejected this holding, explaining that to demonstrate exclusion, a potential competitor such as Biovail must demonstrate "both its intention to enter the market and its preparedness to do so" (citing *Hecht v. Pro-Football*, 570 F.2d 987, 994). Here, Biovail failed in its pleadings: it did not explicitly allege that it was prepared to bring a generic version of diltiazem to market or that it anticipated FDA approval, and it failed to inform the court when it received FDA approval. That made dismissal of the claim appropriate.

But the district court went further and dismissed with prejudice, deciding that as a matter of law, Biovail could not set forth any facts that would entitle it to relief. Because Biovail could correct this deficiency by pleading its intent and preparedness to enter, the D.C. Circuit decided the district court decision was erroneous.

Andrx posited several other legal grounds to support the dismissal with prejudice. First, it argued that the agreement did not cause any injury because it was the FDA regulatory scheme that kept Biovail off the market. Andrx noted that the successful defense requirement applied when the agreement was entered into, so Andrx would have had exclusivity only if it won its suit. The D.C. Circuit disagreed, noting that the agreement was entered into nine months after the successful defense requirement was struck down.

Andrx turned to more conventional antitrust arguments to defend the agreement, arguing that its restrictions were appropriate under the ancillary restraints doctrine and citing *Polk Bros., Inc. v. Forest City Enters., Inc.*, 776 F.2d 185 (7th Cir. 1985). The court rejected this argument as well, noting that "the Agreement's allegedly anticompetitive provisions, including Andrx's pledge to continue to pursue its ANDA so as to forestall other applicants from receiving final FDA approval, were not necessarily

[7] Id. at 1331–1333.
[8] *In re Cardizem CD Antitrust Litigation*, 105 F. Supp. 2d 682 (E.D. Mich. 2000) (hereinafter *Cardizem*).
[9] 256 F.3d at 805–806.

ancillary restraints but rather could reasonably be viewed as an attempt to allocate market share and preserve monopolistic conditions."

Andrx also argued that there was no restraint because Biovail had other alternatives, including petitioning the FDA to nullify the 180-day exclusivity period. The D.C. Circuit distinguished the cases on which Andrx relied because "Andrx cited no consumer benefit here." In addition, the time for Biovail to exercise any of these alternatives "made this option less than 'fully available.' "

Antitrust Injury

The law requires antitrust plaintiffs to prove "antitrust injury," i.e., injury of the type the antitrust laws were intended to prevent and that flows from that which makes defendants' acts unlawful. Andrx argued that there was no antitrust injury and that the case was akin to *Bruinswick*, which held that competing bowling alleys did not have standing to challenge a bowling alley merger because they would have benefited from any post-merger price increases. The Court rejected Andrx's argument.

Unlike the *Brunswick* plaintiffs' injury, Biovail's alleged injury is the type the antitrust laws were designed to prevent. If Biovail's allegations are correct, the Andrx-HMRI Agreement neither enhanced competition nor benefited consumers; if anything, it accomplished just the opposite by preserving HMRI's monopoly. Moreover, Biovail alleged that its exclusion from the market occurred not only by reason of the unlawful Agreement but also by reason of that which made the Agreement unlawful, that is, an illegal restraint of trade.

Andrx then argued that it could have decided on its own not to market the drug and that would have had the same effect of excluding Biovail. The Court rejected that argument because of the $10 million quarterly payment: "Andrx's argument that any rational actor would wait for resolution of the patent infringement suit is belied by the quid of HMRI's quo."

The D.C. Circuit also rejected Andrx's argument that the agreement merely preserved the status quo and thus was no more than a private stipulated preliminary injunction. According to the Court, even if that was the case, judicial review plays an important role in protecting the public interest—concerns articulated in FTC Commissioner Sheila Anthony's speech on patent settlements. Moreover, the Court noted that even if the settlement was legal, its commitment to prosecute its ANDA and do nothing to jeopardize the 180-day exclusivity period "went beyond the status quo" and were not ancillary. The Court seems to suggest that these provisions indeed may be per se illegal, citing Judge Bork's decision in *Rothery*:

> To be ancillary, and hence exempt from the per se rule, an agreement eliminating competition must be subordinate and collateral to a separate, legitimate transaction. . . . If [the restraint] is so broad that part of the restraint suppresses competition without creating efficiency, the restraint is, to that extent, not ancillary.

Rothery Storage & Van Co. v. Atlas Van Lines, Inc., 792 F.2d 210, 224 (D.C. Cir. 1986), cited in *Andrx v. Biovail*, 256 F.3d at 814–815.

The remaining issues of injury, speculative nature of the harm, existence of more appropriate plaintiff, and duplicate recovery were straightforward.

Noerr-Pennington

Finally, Andrx argued that the agreement should be protected under the *Noerr-Pennington* doctrine in the same fashion as threatened litigation or an offer of a settlement. The Court disagreed and specifically adopted the reasoning of the district court in the private consumer litigation involving the Andrx agreement. In *Cardizem CD Antitrust Litigation*, 105 F. Supp. 2d 618, 635 (E.D. Mich. 2000), the district court found that the competitive harm was not the result of a court decision. "Rather, it is the result of purely private conduct and thus constitutes a private restraint of trade subject to liability under the antitrust laws." The Court also relied on Judge Posner's decision in *Brand Name Prescription Drugs Antitrust Litigation*, 186 F.3d 781, 789 (7th Cir. 1999) ("[T]he doctrine does not authorize anticompetitive action in advance of government's adopting the industry's anticompetitive proposal. The doctrine applies when such action is the consequence of legislation or other governmental action, not when it is the means for obtaining such action (or in this case inaction).").[10] The D.C. Circuit observed that this Agreement was "not unlike a final, private settlement agreement resolving the patent infringement litigation by substituting a market allocation agreement" and that type of agreement would not enjoy *Noerr-Pennington* immunity.

[10] Cited in Andrx at 256 F.3d at 818.