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MEDICARE AMENDMENTS PRESERVE STRATEGIC OBSTACLES FOR GENERICS

In the 2003 Medicare Prescription Drug, Improvement and Modernization Act (the "Medicare Amendments"), Congress addressed a "critical" issue for generic drug companies — when a company that files an abbreviated new drug application (ANDA) seeking to market a generic formulation can bring an action against the innovator company for a declaratory judgment of patent noninfringement or invalidity. Despite an explicit provision in the legislation authorizing declaratory judgment actions as well as presumed congressional intent to foster such actions, the Federal Circuit, in *Teva v. Pfizer*, found that Congress did not intend to modify the jurisdictional test applied in a traditional patent infringement suit. Accordingly, the court held that no declaratory judgment action could be brought by the generic company absent a traditional threat of suit for patent infringement. With three judges dissenting, the Federal Circuit recently denied a rehearing and rehearing en banc of that decision. The Federal Circuit has thus thwarted the ability of generic companies to use declaratory judgment actions to clear marketing bottlenecks that can result when an innovator chooses to defer or delay suit.

Under the Hatch-Waxman Act, pharmaceutical companies can obtain an automatic 30-month stay of approval of an ANDA for a competitive generic product by filing suit against the ANDA applicant within 45 days after receipt of a Paragraph IV certification — a letter from the applicant asserting that its product will not infringe the patent or patents listed as claiming the drug covered by the new drug application (NDA) in the FDA publication known as the "Orange Book," or asserting that the listed patent or patents are invalid. In a new section entitled "Civil Action to Obtain Patent Certainty," the Medicare Amendments provide the ANDA applicant the right, "to the extent consistent with the Constitution," to bring a declaratory judgment action should the patentee fail to sue within 45 days. The *Teva* decision turned on the constitutional prerequisites for declaratory judgment jurisdiction in the Hatch-Waxman context.

Pfizer is the owner of the '518 patent covering sertraline hydrochloride, the active ingredient in the antidepressant Zoloft®, as well as a later-expiring '699 patent covering a particular crystalline (or polymorphic) form of sertraline hydrochloride. Six ANDA applicants filed Paragraph IV certifications claiming that the '699 patent was invalid and/or not infringed by their formulations; none challenged the '518 patent. Pfizer sued only Ivax, the first company to file an ANDA, and then reached a settlement permitting Ivax to enter the market upon the expiration of the '518 patent, subject to payment of a royalty. As the first filer, Ivax is entitled to a 180-day period of generic marketing exclusivity during which no subsequent ANDA (e.g., Teva's) may be approved. Under the older rules applicable to Ivax's ANDA, the 180-day exclusivity period begins on the earlier of the first commercial marketing of a generic product or a court decision. Thus, unless Pfizer sues a second generic company, there will be no court decision, and Ivax's exclusivity period will not commence until it chooses to begin marketing its products after the '518 patent has expired.

Hoping to obtain a judgment and thus precipitate the earlier running of the 180-day period, Teva filed a declaratory judgment

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BIO 2005

THANK YOU FOR ATTENDING

It was a pleasure seeing so many of you at BIO 2005 in Philadelphia — it proved, yet again, to be a successful conference in the life sciences industry. To the nearly 250 clients and contacts attending our reception and over 400 attending our panel discussions, we thank you for sharing part of your conference experience with Morgan Lewis and look forward to seeing you next year in Chicago for another great event.

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15–16 MEDTECH INVESTING EUROPE
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DECEMBER

12–14 AMERICAN CONFERENCE INSTITUTE 10TH ANNUAL DRUG AND MEDICAL DEVICE LITIGATION CONFERENCE
NEW YORK

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action against Pfizer for noninfringement and invalidity of the '699 patent. The district court dismissed the action for lack of declaratory judgment jurisdiction. On appeal, the Federal Circuit, with Judge Mayer dissenting, found that Teva had not shown the requisite "actual controversy" under the Declaratory Judgment Act, 28 U.S.C. § 2201, and Article III of the Constitution, to establish jurisdiction.

The Federal Circuit began its analysis with the two-part inquiry that the court had developed to determine whether an actual controversy exists in a patent infringement action: (1) reasonable apprehension of an infringement suit; and (2) present activity by the plaintiff that could constitute infringement or concrete steps taken with the intent to conduct such activity. Because Pfizer and Teva agreed that the latter part of the test had been met, the court focused on the first part. Teva argued that it had a reasonable apprehension of suit by Pfizer. Alternatively, Teva argued that the test was not constitutionally required and had been modified or eliminated by the Medicare Amendments.

First, Teva contended that Pfizer's listing of the '699 patent in the Orange Book (by which Pfizer represented that the patent "could reasonably be asserted" against any generic sertraline product) and Pfizer's failure to sue Teva, or affirmatively to represent that it would not sue Teva, provided the necessary threat of suit. However, the court found Pfizer's listing of the patent to be a statutory requirement, and thus that Teva had established nothing more than that there existed an adversely held patent. Pfizer's failure to grant a covenant not to sue was not dispositive.

Further, the court held that Teva had to demonstrate a "reasonable apprehension of *imminent* suit" (emphasis added), a requirement the court inferred from the mandate of Article III that the injury be "concrete" and "actual or imminent." By importing an imminency requirement, the Federal Circuit dictated the result, as Teva "virtually concede[d] that Pfizer will not bring immediate suit." Pfizer had no need to initiate an immediate suit because Teva could not market its product until at least 180 days after expiration of the '518 patent in June 2006. Indeed, as Judge Dyk pointed out in his dissent from the denial of rehearing, declaratory judgment jurisdiction was designed for situations where the defendant patentee declined to bring suit, so such suit would, by definition, not be imminent.

Turning to the Medicare Amendments, the court examined the statutory language and legislative history to determine if the standard had changed. The court interpreted the statutory requirement that a declaratory judgment action be brought "consistent with the Constitution" to indicate that Congress did not intend to alter the usual test. It found additional support for its interpretation in the discussion of the jurisdictional requirements in the legislative history:

> Through the modifications in this Act, the conferees do not intend for the courts to modify their application of the requirements under Article III that a declaratory judgment plaintiff must, to the extent required by the Constitution, demonstrate a "reasonable apprehension" of suit to establish jurisdiction.
>
> * * *
>
> In determining whether a reasonable apprehension of suit exists where an ANDA has been filed with a paragraph IV certification and the patentee has not brought an infringement suit within the 45 days, the conferees expect courts to examine these specific factors as part of the totality of the circumstances. . . . In any given case, the conferees expect a court may or may not find a reasonable apprehension of suit where these two specific factors are present.

H.R. Conf. Rep. No. 108-391, at 836 (2003) (citations omitted).

In contrast, Teva pointed to the statement in the Committee report that a court's analysis was to be informed by the "particular policies served by the Hatch-Waxman Act," and contended that its inability to challenge the '699 patent and gain access to the market during the 180-day exclusivity period caused an injury that was a sufficient predicate for suit. Rejecting this argument, the court noted that an earlier draft of the Medicare Amendments had language, omitted from the final version, that would have conferred jurisdiction anytime a Paragraph IV certification was filed and the NDA holder did not sue within 45 days. The court found Pfizer's actions permissible under Hatch-Waxman, and left it to Congress to address any inequities caused by the legislation.

In his dissent, Judge Mayer contended that the two-part test applied by the majority was not constitutionally mandated. Although Judge Mayer agreed with the majority that Congress had apparently blessed the need to show reasonable apprehension of suit to establish jurisdiction, he concluded that this requirement should be applied differently in the Hatch-Waxman context, where, unlike in an ordinary patent suit, the putative infringer is not free to market its product in the face of an adversely held patent. Considering the

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*Morgan Lewis' Life Sciences Practice is one of the largest in the nation, with approximately 200 lawyers whose practice and experience are significantly devoted to the life sciences industry. Additionally, we have more than 200 professionals with life sciences scientific degrees, nearly a third of whom have advanced degrees. For more than two decades, we have developed our practice to "**protect the complete life sciences product life cycle**," with depth and quality in all important areas: regulatory, transactional and litigation. For more information regarding Morgan Lewis' Life Sciences Practice, please contact the group's Chair, Stephen Paul Mahinka, at 202.739.5205 or smahinka@morganlewis.com.*

Drug Patents May Not Bar Rival Research After *Merck v. Integra*

In June 2005, the U.S. Supreme Court issued the long-awaited ruling on the dispute between Merck KGaA and Integra Life Sciences Holdings Corp. over the unlicensed use of patented compounds in research and development. While the Supreme Court affirmed the position that many drug developers had adopted years ago — that they are free to use patented compounds in development without a license — it also extended this right upstream from clinical development to earlier-stage research, while at the same time expressly avoiding any discussion about the application of the exemption to "research tools."

The Supreme Court was interpreting a clause in the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, that was originally promulgated to allow companies to make and test drugs in anticipation of the drugs coming off patent, under the theory that this would allow generic drugs to be brought to market sooner. This clause, 35 U.S.C. § 271(e)(1), which is also referred to as the "safe harbor," allows a company to infringe another's patent as long as its use of the invention is reasonably related to the development and submission of information to the FDA. The lower appellate court, the Court of Appeals for the Federal Circuit, had interpreted this to allow for clinical research using patented drugs. However, the Supreme Court opted for a broader interpretation, stating that Congress intended that the safe harbor provision extend "to all uses of patented inventions that are reasonably related to the development and submission of any information" under the Food, Drug and Cosmetic Act. Hence, the Supreme Court did not limit the safe harbor to activities that provide data in an FDA submission, but adopted a more expansive view, specifically identifying preclinical pharmacological, toxicological, pharmacokinetic and biological studies of a drug in animals and research relating to risk-benefit analyses as being within the safe harbor.

At the same time, the Supreme Court attempted to set some parameters to help determine which preclinical research activities fall within the safe harbor. Thus, on the one hand, the exemption does not include "[b]asic scientific research on a particular compound, performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce." On the other hand, the exemption applies "[a]t least where the drugmaker has a reasonable basis for believing that a patented compound may work, through a particular biological process, to produce a particular physiological effect, and uses the compound in research that, if successful, would be appropriate to include in a submission to the FDA." Thus, the safe harbor is extended to research in which there is a "reasonable basis for belief" that the particular drug will produce a physiological effect and the research will be submitted if it is successful, but not research without "intent" to develop a "particular drug." Accordingly, the scope of the exemption turns on how the phrases "intent to develop," "particular drug" and "reasonable belief" will be construed — a key question will be how many drugs can be screened and still be considered research regarding a "particular drug."

What does the decision mean for research tools? The Supreme Court could have stated that application of § 271(e)(1) to the use of a research tool will be judged by the guidelines offered in the opinion. It explicitly did not. By avoiding such a statement, the Supreme Court expressly left open whether research tools will be exempt even when used in the context of exempt research.

However, the decision may nonetheless be instructive for some research tools. The Supreme Court does not define the term "research tools" beyond concluding that the RGD peptides at issue were not being used as research tools by Merck. The Supreme Court specifically noted in a footnote that it was not "express[ing] a view about whether or to what extent § 271(e)(1)" exempts research tools used in the development of information for the regulatory process. Although the Court of Appeals for the Federal Circuit thought this question was a necessary part of its decision, the Supreme Court found that it did not need to decide where research tools fell in the development process because the RGD peptides were not used as research tools by Merck, and Integra had not argued that they had been so used. Some might quarrel with that conclusion. Scripps Research Institute used the RGD peptides on Merck's behalf to screen potential compounds and identify the best one, which suggests that they were being used as research tools. Indeed, notwithstanding the Supreme Court's characterization of Integra's position, Integra's brief to the Supreme Court states that "Merck paid Scripps to use Integra's patented invention as a 'tool.'" Thus, the applicability of the safe harbor to research tools will have to include and will be largely driven by the definition of "research tool" adopted by the courts.

What does this mean to most biotech and pharmaceutical companies? Most companies were already operating under the assumption that drug development was exempt; the companies that were most concerned with the outcome of this case were the research tool companies. In light of the opinion, research companies should consider revisiting their patent strategies to make sure that appropriate and separate coverage exists for research tools and drug products. They should also review marketing and commercial positions to ensure that they clearly distinguish between research tools and drug products in brand management as well as in company presentations. Finally, research companies need to be sensitive to this issue when entering into licensing arrangements so that a clear distinction is made between drug development and research conducted with the assistance of research tools.

For more information, please contact Manya S. Deehr, a partner in the firm's Business and Finance Practice, at 609.919.6664 or mdeehr@morganlewis.com, or Janet B. Linn, a partner in the firm's Litigation Practice, at 212.309.2110 or jlinn@morganlewis.com.

Morgan Lewis is pleased to announce that Michael J. Holston and Lisa C. Dykstra have joined our Litigation Practice resident in our Philadelphia office. Michael is a former assistant U.S. attorney, and focuses his practice on complex civil litigation, primarily defending products liability and consumer fraud class-action lawsuits, and white-collar criminal defense litigation. Lisa, also a former assistant U.S. attorney, focuses her practice on government investigations, internal investigations and litigation involving claims of fraud and abuse.

Both Michael and Lisa are a welcome addition to our Life Sciences and Product Liability Litigation Practices.

To view Michael Holston's and Lisa Dykstra's full biographies or for additional information, please visit www.morganlewis.com.

MEDICARE AMENDMENTS

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marketing delay and the "real and defined harm" resulting from uncertainty traceable to Pfizer's conduct, Judge Mayer found that there was reasonable apprehension of suit under the circumstances sufficient to confer declaratory judgment jurisdiction.

The Federal Circuit subsequently denied rehearing and rehearing en banc, with Judges Dyk, Mayer and Gajarsa dissenting. Judges Dyk and Gajarsa each filed separate dissenting opinions that the other joined. Both considered reasonable apprehension of suit an inappropriate test for injury in the Hatch-Waxman context, and one that was not constitutionally mandated notwithstanding any language to the contrary in the legislative history.

Judge Gajarsa, calling the issue a critical one, decried the fact that the decision allows "statutory procedures to be manipulated by the patent holders." As Judge Gajarsa noted, unlike in typical patent infringement litigation where the uncertainty of legal rights resulting from the threat causes harm, the injury existed independent of any such threat in the Hatch-Waxman context. Rather, he found that Teva suffered a "concrete, actual or imminent injury" from Pfizer's conduct insulating the '699 patent from a validity challenge, precluding the FDA from approving Teva's generic product until 180 days after Ivax's exclusivity period expired, and allowing Pfizer, by avoiding an explicit threat, to create a bottleneck and "simply ride out the term of the listed patent."

Similarly, Judge Dyk noted that the language of the legislation allowed jurisdiction to the full extent of Article III and found that the timing of approval of Teva's ANDA constituted a present concrete controversy sufficient to establish jurisdiction.

The Federal Circuit thus split between the majority, who considered the test for an Article III actual controversy imported from the typical infringement action to be constitutionally mandated, and the dissenters, who found an actual controversy inherent in the marketing bottleneck facing Teva. The split was fostered by Congress's attempt to straddle the two positions. The statutory language offers no standard beyond the amorphous "consisten[cy] with the Constitution," and the legislative history is equivocal. On the one hand, Congress directed a court to consider the "specific factors" of the Hatch-Waxman situation in its jurisdictional analysis. However, it also stated that a court "may or may not find a reasonable apprehension of suit" where these factors are present, thus approving the reasonable apprehension requirement, but allowing courts to ignore the "specific factors" they were directed to consider.

In sum, the majority of the court considered Pfizer's actions to be permissible under Congress's statutory scheme notwithstanding any injury to Teva, and determined that there was no mandate from Congress to allow a declaratory judgment challenge based on marketing delay. Moreover, as the court acknowledged, ANDAs filed after December 8, 2003 (the effective date of the Medicare Amendments) are subject to the new provisions enacted to eliminate manipulation of the 180-day exclusivity period. Nonetheless, it is clear that there will be situations in which a declaratory judgment action could speed generic approval, but such actions, absent some clear threat by the innovator, will be dismissed under the Federal Circuit analysis.

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SPEECHES

Pharmaceuticals/Biotechnology/ Medical Devices

TOPRA Annual Symposium 2005
Data (or Market) Exclusivity
Anthony Warnock-Smith
October 6, 2005, Berlin

American Conference Institute 10th Annual Drug and Medical Device Litigation Conference
Preparing for Plaintiffs' Latest Theories & Claims: In-House & Outside Perspectives
James D. Pagliaro
December 13, 2005, New York

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