AUGUST
2005

HEALTH CARE AND LIFE SCIENCES PRACTICE
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Health Care & Life Sciences
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Supreme Court Clarifies, And Seems To Weaken, Patent Rights In Pharmaceutical Compounds

On June 13, 2005, the United States Supreme Court announced its decision in *Merck v. Integra Lifesciences*, holding that the use of patented compounds in preclinical research may be protected under the "FDA exemption" to patent infringement contained in 35 U.S.C. § 271(e)(1).[1] The *Merck v. Integra* decision has significant implications for holders of patents on chemical compounds, permitting the use of patented compounds so long as such use is reasonably related to the development and submission of *any* information under the Food, Drug & Cosmetic Act. This permitted use provides an opportunity for competitors to design around the patent or to develop improvements to the patented innovation. In light of the Supreme Court's decision in this case, entities involved in the development of chemical compounds as drug candidates must reassess their strategies for protecting their intellectual property.

The Court's Decision

At issue before the Court was the scope of the safe harbor afforded by 35 U.S.C. § 271(e)(1). This section of the Patent Act was enacted in 1984 as part of the Drug Price Competition and Patent Term Restoration Act ("Hatch-Waxman Act").[2] Also known as the "FDA-exemption" and the "Bolar Amendment", it was added to the Hatch-Waxman Act in response to the decision of the Federal Circuit in *Roche Products, Inc., v. Bolar Pharmaceutical Co.*,[3] holding that the common law experimental use exception did not protect even limited use of a patented drug by a generic drug manufacturer for the purpose of meeting FDA's drug approval requirements. The amendment was intended to ensure the rapid entry of generic drugs onto the market upon expiration of a brand drug's patent and permitted "experiments in advance of the patent expiration as long as those activities were reasonably related to securing regulatory approval."[4]

Title 35 U.S.C. § 271(e)(1) provides that "[i]t shall not be an act of infringement to…use…or import into the United States a patented invention solely for purposes reasonably related to the development and submission of information under a Federal law which regulates the …use …of drugs." Rejecting the position

[1] *Merck v. Integra Lifesciences*, No. 03-1237 (June 13, 2005). The Court reversed the decision of the United States Court of Appeals for the Federal Circuit holding that the "FDA exemption" to infringement did not apply to the preclinical research activities alleged by Integra to infringe their patents, and remanded the case for further consideration consistent with its reading of the statute.

[2] Pub. L. No. 98-417, 98 Stat. 1585 (1984).

[3] 773 F.2d 858 (Fed. Cir. 1984).

[4] *Integra Lifesciences v. Merck KGaA* 331 F.3d 860, 865 (Fed. Cir 2003).

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of the Federal Circuit that Merck's activities were not protected by the safe harbor because preclinical research activities are not reasonably related to submissions for FDA approval, the Supreme Court held that the plain language of the statute precludes such a narrow interpretation. Instead, the Court stated that "§ 271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of *any* information under the [Food, Drug & Cosmetic Act]…This necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process."[5]

The Supreme Court rejected Integra's argument that the only preclinical data of interest to the FDA is that relating to the compound's safety, reasoning that the FDA requires submission of "summaries of the pharmacological, toxicological, pharmacokinetic, and biological qualities of the drug in animals" for consideration in the Agency's overall risk-benefit analysis.[6] "Such information necessarily includes preclinical studies of a drug's efficacy in achieving particular results." The Court further rejected arguments that preclinical research that was not conducted according to good laboratory practice regulations is ineligible for protection under § 271(e)(1), as these regulations do not apply to preclinical efficacy testing.[7]

Despite its extension of the scope of § 271(e)(1), the Supreme Court's decision was not without limitation. It stated that "[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, is surely not 'reasonably related to the development and submission of information to the FDA.'"[8] The Court further refused to extend the exemption to cover the use of research tools in preclinical research, rather than the use of patented compounds themselves, as this type of invention was not at issue in the case.

Reversing the Federal Circuit's interpretation of the exemption, the Supreme Court held that "(1) experimentation on drugs that are not ultimately the subject of an FDA submission [and] (2) use of patented compounds in experiments that are not ultimately submitted to the FDA" are not excluded from the exemption in § 271(e)(1). This decision represents a broad reading of the section, the result of which is to protect much of industry's use of patented compounds in preclinical research. "At least where a 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,

[5] *Merck v. Integra Lifesciences*, No. 03-1237, slip op. at 8 (June 13, 2005) (emphasis in original).

[6] *Id.* at 9.

[7] *Id.* at 11. The Court further noted that even preclinical safety testing that is not conducted in compliance with these regulations may be submitted to the Agency if the submission includes a "brief statement for the noncompliance." (*quoting 21 CFR § 58.1(a)*).

[8] *Id.* at 12.

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would be appropriate to include in a submission to the FDA, that use is 'reasonably related' to the 'development and submission of information under …Federal law.'"[9]

Implications for Holders of Chemical Entity Patents and Strategies Moving Forward

As a result of the Court's decision in this case, patents on chemical compounds subject to FDA approval have lost much of their ability to confer a strategic advantage. The question is how much, and therein lies a large part of the problem because uncertainty effects strategic decisions. Patent applications are published eighteen months after filing, providing a competitor with sufficient information to initiate research on improvements on the compound before the original patent has issued. Holders of existing patents will be unable to bring infringement actions in many instances in which they otherwise would have sought protection for their intellectual property in the courts. By reevaluating their patent preparation, prosecution and litigation strategies in light of the current legal environment, companies can maximize the protection of their intellectual property.

It is well established that the disclosure of a species prevents a later genus claim, (it may not prevent other species claims).[10] Predictability is less certain where the first disclosure purports to be the genus. This will depend upon the size of the genus compared to the level of the disclosure. Even with a high level of disclosure, the new species may still be patentable if it produces results unexpectedly different than that of other previously known members of the genus.

Thus, to limit the development and protection of improvements by competitors, patent applicants should ensure that the disclosure and claims are drafted broadly enough to include for example all potential polymorphs of the patented compounds. (Polymorphism is the phenomenon where a compound can precipitate to form numerous crystal structures. The different crystalline structures each have different physical properties, which can change the use of the chemical.) For example, exploration of polymorphism in multiple salts through the use of high throughput experimentation and various spectroscopic techniques can influence the choice of salt forms, aiding in the identification and advancement of preferred development candidates. This may aid in maximizing product extension opportunity and strength of resulting intellectual property protection.

As additional research efforts will be required to obtain the information necessary to meet this level of disclosure and draft these claims, an applicant may wish to pursue a provisional application to provide an additional year of

[9] *Id.* at 13-14.

[10] A genus is a class or group with common attributes while a species is an object or item within that class. For example, the genus halogen comprises the species: Fluorine, Chlorine, Bromine, Iodine, and Astatine. The common attribute is that they each have 7 electrons in their outer shells, giving them an oxidation number of -1. Halogen is an example of a very small genus, some genus comprise hundreds of species.

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confidentiality in which to complete this work.[11] The Patent Act provides for the filing of a provisional patent, including only the specification, names of the inventors and any necessary drawings. Claims are not required and the application is not reviewed. A provisional application may serve as the priority document upon which the complete U.S. and/or PCT patent application may be filed within the next twelve months. The patent term, however, will run only from the date of the complete application. Provisional patent applications are not published, thus, their use may extend the period in which an applicant may maintain its invention in secret, without the loss of filing priority.

Conclusion

Applying for a provisional application to allow for additional research supporting a more broadly written specification is one possible strategy to preserve some of the certainty patent holders had prior to the Supreme Court's decision in *Merck*. However, any responsible approach to protecting one's intellectual property rights and portfolio must include exploring other legal options to enhance strategic flexibility and advantage.

* * *

If you would like additional information regarding this topic, please contact Gianna Arnold, in the firm's Washington, DC office at 202/861-1379, email garnold@ebglaw.com; Amy Dow, in the firm's Chicago office at 312/499-1427, email adow@ebglaw.com or James Flynn, in the firm's Newark office at 973/639-8285, email jflynn@ebglaw.com or the Epstein Becker & Green attorney who regularly handles your legal matters. For further information about Epstein Becker & Green's Health Care & Life Sciences Practice, or to see back issues of Special Alerts, please visit our website at www.ebglaw.com.

Members of the Life Sciences and Intellectual Property Subgroups prepare and prosecute patents, provide opinions on infringement and validity issues, provide transactional services including licenses, joint development agreements, and cooperative research agreements; and counsel clients concerning various intellectual property issues.

[11] 35 U.S.C § 111(b) provides for the filing of a provisional application.

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