The US Supreme Court recently confirmed that a company may use another company’s patented inventions to conduct testing in advance of the patent’s expiration, that is “reasonably related to the development and submission of any information” required under the Federal Food, Drug, and Cosmetic Act (FDCA). Merck KGaA v. Integra Life Sciences I, Ltd., 125 S. Ct. 2372 (2005). In Merck, the Court interpreted broadly the safe harbor provided by 35 U.S.C. § 271(e)(1) to permit the use of a patented compound in pre-clinical and clinical studies of a drug candidate’s safety, pharmacologic effects and mechanism of action, that are reasonably related to the development of information for submission to the Federal Food and Drug Administration (FDA) even if the compound is not ultimately the subject of an FDA submission or if the results are not included in the submission to the FDA.

Background
In general, it is an act of patent infringement “to use[] a patented invention during the term of the patent.” 35 U.S.C. § 271(a). Before the passage of the Hatch-Waxman Act in 1984 (and the addition of 35 U.S.C. § 271(e)(1) to the patent code), no one, except the patent holder and its licensees, could make or use a patented compound to conduct drug research to develop other useful drugs. With the enactment of Hatch-Waxman, Congress created an exemption from this general rule, codified at § 271(e)(1), that provides in pertinent part:

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention ... solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use or sale of drugs.

The Merck Case
In Merck, the Supreme Court addressed when studies using a patented drug constitute a “use[] reasonably related to the development and submission of information” required by the regulatory process for FDA drug approval. The case involved testing conducted on a tripeptide sequence known as RGD peptide that had been patented by Integra. A researcher for the Scripps Research Institute discovered that certain patented peptides (“RGD peptides”) inhibited angiogenesis (the process by which new blood vessels develop from existing vessels) and had the potential to inhibit the growth of cancerous tumors by blocking receptors needed for the tumors’ blood vessel growth. Following that discovery, Merck
entered into a 3-year agreement with Scripps to identify potential drug candidates by experimenting with RGD peptides. Integra then sued Merck and Scripps for patent infringement.

After the trial, the jury found that Merck and Scripps had infringed Integra’s patents, and awarded damages of $15 million. On post-trial motions, the District Court dismissed the suit against Scripps and its researcher, but affirmed the judgment of infringement and damages against Merck. The trial court concluded that there was insufficient evidence to establish the connection between the infringing experimental use and FDA review to fall within § 271(e)(1)’s statutory exemption.

On appeal to the Federal Circuit, Merck argued that the District Court had erroneously interpreted the scope of activities protected by § 271(e)(1). The Federal Circuit nonetheless affirmed. It found that the Scripps’ work sponsored by Merck was not clinical testing conducted to supply information to the FDA, but was instead “general biomedical research” intended to identify, among several lead candidates, new drugs that may be subsequently subject to future clinical testing to support an FDA application. Thus, the Federal Circuit concluded that the Merck-Scripps research on RGD peptides was too attenuated from the FDA approval process to be considered “reasonably related” to the development and submission of data for the FDA. Consequently, the Federal Circuit held that the testing conducted by Scripps for Merck fell outside the safe harbor of § 271(e)(1).

The Supreme Court granted Merck’s petition for certiorari, and reversed the Federal Circuit’s judgment. The Supreme Court ruled unanimously that the Federal Circuit had construed the scope of activities protected by § 271(e)(1) too narrowly. The Court found that the “statutory text makes clear that it provides a wide berth for the use of patented drugs in activities related to the federal regulatory process.”

In reaching its decision, the Court recognized the expansive coverage of the FDA regulatory process. The Court emphasized that the exemption at 271(e)(1) applies to “all uses of patented compounds ‘reasonably related’ to the . . . develop[ment of] information for submission under any federal law regulating the manufacture, use or distribution of drugs.” Merck, 125 S. Ct. at 2383 (emphasis in the original). The Court explained that the exemption extends beyond merely testing an active ingredient to support an Abbreviated New Drug Application (ANDA) to market a generic version of a new drug. It also includes in vivo and in vitro preclinical testing which, if successful, could support an Investigational New Drug (IND) application to FDA for approval to conduct human clinical testing, as well as later stage preclinical and clinical testing to support a New Drug Approval (NDA) application.

Recognizing the inherent uncertainty in the identification of a successful drug candidate and the need “for adequate space for experimentation and failure on the road to regulatory approval,” the Court held that the exemption permits testing “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 where the testing, if successful, would be appropriate to include in a submission to the FDA.” Such activities “necessarily include[] preclinical studies of patented compounds,” related to a drug’s safety, efficacy, mechanism of action, pharmacokinetics and pharmacology, such as the studies that Scripps conducted on the RGD peptide.

The Supreme Court, however, cautioned that the statutory exemption does not embrace all experimental activities “performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the research intends to induce.”
Nonetheless, the Court clarified that § 271(e)(1) does not necessarily exclude:

(1) experimentation on drugs that are not ultimately the subject of an FDA submission, nor
(2) the use of patented compounds in experiments not ultimately submitted to the FDA.

To the contrary, given that § 271(e)(1) “exempt[s] from infringement all uses of patented compounds ‘reasonably related’ to the process of developing information for submission of any federal law regulating the manufacture, use or distribution of drugs” (emphasis in the original), the Court found that “the exemption is sufficiently broad to protect the use of patented compounds in both situations.”

The Court recognized the uncertainties of the new drug development process, in which few of the potential new drug candidates that are tested ultimately receive NDA approval and a researcher cannot know in advance which potential new candidates may ultimately prove successful. Thus, to limit testing to compounds on which an IND ultimately is filed would effectively limit preclinical testing to that required to support an ANDA for a generic version of an existing drug. This the Court declined to do.

Moreover, the Court observed that the use of a patented compound in experiments, the results of which are not included in a “submission of information” to the FDA, may nevertheless fall within the scope of § 271(e)(1) if “there is a reasonable basis for believing that the experiments will produce ‘the types of information that are relevant to an IND or NDA.’” Factors such as the “extent to which [a patented drug] has been studied previously” and “the known or suspected risks of the drug” may influence the amount of information that must be submitted in an IND application, and thus, such results, even if unreported, could be considered “reasonably related” to the “develop[ment] of information for submission” to the FDA. In these circumstances, the Court’s expansive reading of the 271(e)(1) exemption permits extensive pre-clinical and clinical safety, effectiveness, mechanistic, pharmacokinetics and pharmacology testing to support the drug development process, even if the results fail to demonstrate the pharmacologic benefit of the candidate and even if the information is not itself ultimately submitted to the FDA.

The Court left unanswered whether and to what extent § 271(e)(1) exempts from infringement “research tools” used in the development of information required for the drug regulatory process. Arguably, patented compounds, by themselves, may be viewed as research tools in certain circumstances because they may “pave the way,” for instance, to other new and improved drugs. In view of the Court’s broad reading of § 271(e)(1) in Merck, patented research tools, in general, might come within the statute’s safe harbor, provided they are used with the requisite intent and purpose.

Lessons For Drug Researchers

Merck brings welcome relief to pharmaceutical companies seeking to develop new drugs, derived from a patented compound held by another company. The Court’s decision makes clear that permissible testing is not limited to that which would be required to support an ANDA for a generic version of a previously approved drug.

According to the Court, the exemption at 271(e)(1) permits companies to conduct testing of unapproved patented compounds without a license from the patent holder – provided they have a “reasonable basis” to believe either that (1) the patented compound may work to produce a particular intended physiological effect or (2) the experiments will produce the types of information that are relevant to an IND or NDA, including pre-clinical in vivo and in vitro experiments. Thus, the
patented compound being tested does not necessarily have to be the subject of a submission to FDA and the data need not necessarily be included in an FDA submission for testing on the compound to be exempt from infringement pursuant to 271(e)(1). Use of another’s patented compound, however, remains outside the scope of exemption when there is no “intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the research intends to induce.” Whether section 271(e)(1) applies to “research tools” in general remains an open question.

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