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Intellectual Property

Supreme Court Broadly Construes Research Exemption from Patent Infringement

In a patent infringement suit closely watched by many connected to the biotechnology and pharmaceutical industries, the United States Supreme Court recently issued a unanimous decision in *Merck KGaA v. Integra LifeSciences I, Ltd.*, No. 03-1237, (S.Ct. June 13, 2005). The decision broadly interprets the scope of the Patent Act's safe harbor exemption from patent infringement to include certain preclinical research and development activities, whether or not ultimately the subject of an FDA submission, "as long as there is a reasonable basis for believing that the experiments will produce 'the types of information that are relevant to an IND [Investigational New Drug application] or NDA' [New Drug Application]". Slip Opinion at 14 (quoting the Brief of the United States as Amicus Curiae). The Court, however, specifically declined to address an issue of interest to many in the biotechnology community: whether or not the exemption applies to infringement of patents relating to research tools in the development of information for FDA submissions.

The decision also suggests in several passages that the intent of the researcher and the researcher's belief that the patented invention acts through particular biological processes and has particular pathological effects are relevant to the question whether that research may benefit from the exemption to patent infringement.

The case arose when the patent owners, Integra Lifesciences and the Burnham Institute, filed a patent infringement suit against Merck KGaA and others, alleging that research funded by Merck infringed the Integra patents. The research involved the use of various compositions, including components and methods covered by the Integra patents, in a procedure shown to reverse tumor growth in chick embryos.

Based on the success of that research, Merck agreed to expand the research to develop a similarly acting drug for humans, with a view toward eventually submitting an IND to the FDA. In defense, Merck argued, among other things, that it was exempt from infringement under a safe harbor provision of the Patent Act that allows research where information is to be submitted to the FDA. The Integra compositions were not ultimately the compositions chosen for the IND submission, but they were used as positive controls in the research. The District Court and the Court of Appeals for the Federal Circuit ruled in the patent owners' favor, finding infringement and holding that Merck's activities did not fall within the exemption. Merck sought Supreme Court review, setting the stage for the Court's consideration of the statutory exemption, Patent Act Section 271(e)(1).

Under Section 271(a) of the Patent Act, 35 U.S.C. et seq., it is generally an act of patent infringement to "mak[e], us[e], offe[r] to sell, or sel[l] any patented invention ... during the term of the patent therefor" in the absence of the consent of the patent owner. In 1984, Congress enacted the Hatch-Waxman Act, formally known as the Drug Price Competition and Patent Term Restoration Act of 1984, which included an amendment to Section 271 of the Patent Act exempting from infringement certain specific research activities. Section 271(e)(1), in relevant part provides:

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 or veterinary biological products. (Emphases added).

A principal component of the federal framework requiring submission of information relating to the

manufacture, use, or sale of drugs is the Federal Food, Drug, and Cosmetic Act (FDCA). Under the FDCA, drug manufacturers must request FDA approval to perform human clinical trials by submitting an investigational new drug application (IND). The IND must describe preclinical testing of the drug that is “adequate to justify the proposed clinical testing.” Also, before FDA will authorize a manufacturer to market a new drug, the manufacturer must submit a new drug application (NDA) to FDA, which must include results of investigations that have been performed to determine whether or not a drug is safe and effective in use. An NDA must include all clinical studies, and also must provide any preclinical studies showing the efficacy, toxicity, and pharmacological properties of the drug.

The Hatch-Waxman Act, as the statutory title suggests, was intended, in part, to speed to market competitive drugs by allowing some research using the patented inventions of another during the patent term. The commercial manufacture and sale of a drug thus developed, however, can not legitimately occur until after the relevant patent expires. Until the passage of the Hatch-Waxman Act, research to develop new drugs that involved use of a patented invention could not begin unless the researcher obtained a license under the patent, or purchased a commercially available patented compound, or until the relevant patent expired. A delay in starting research necessarily delayed the introduction of new and competitive drugs to the market. An objective of the Section 271(e)(1) exemption is to allow drug manufacturers to perform the clinical and preclinical work necessary to prepare and submit the IND and NDA for a drug without the risk of infringing others’ patents.

Understanding the boundaries of the infringement exemption under the Section 271(e)(1) exemption is of vital importance to concerns engaged in the development and evaluation of new uses for drugs and therapeutic biologicals. Absent such an understanding, companies risk liability for patent infringement and the loss of the very substantial capital investment and effort commonly expended in developing new uses for existing drugs and biologicals. Despite the critical significance of firmly understanding the scope of the exemption, the wording of the section is not precise. Moreover, the scope of the safe harbor has been largely unsettled

since the Federal Circuit’s decision in the *Integra/Merck* controversy, *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003), in which the appeals court rather narrowly interpreted the exemption’s applicability to pre-clinical activities. The Federal Circuit framed the issue before it as whether the Section 271(e)(1) exemption extended as far back down the “chain of experimentation” as the “development and identification of new drugs that will, in turn, be subject to FDA approval.” It seems reasonable to assume that Congress did not intend Section 271(1)(e) as a blanket exemption of any and all pre-commercial activities related to a drug that is approved for marketing by FDA. The Federal Circuit, however, held that there must be a relatively direct relationship between the activity alleged to infringe and the submission of experimental data to FDA, and that the exemption did not include “general biomedical research to identify new pharmaceutical compounds.” The Federal Circuit stated that the exemption “does not globally embrace all experimental activity that at some point, however attenuated, may lead to an FDA approval process. The safe harbor does not reach any exploratory research that may rationally form a predicate for future FDA clinical tests.”

Thus, the Federal Circuit apparently considered activities intended to identify candidate drugs to be submitted for FDA approval as outside the safe harbor since such early stage activities are not, in the words of Section 271(e)(1), “solely for uses reasonably related to the development and submission of information” to FDA. Without such early stage activity, however, it may be impossible to identify candidate drugs warranting the further testing necessary to prepare and submit an IND to FDA.

Against this backdrop, the pharmaceutical industry, the patent bar, and many others in the business and legal communities had eagerly awaited the United States Supreme Court’s decision reviewing the Federal Circuit’s *Integra v. Merck* decision. The Supreme Court broadly interpreted the “solely for uses reasonably related to” language and the scope of the safe harbor under Section 271(e)(1). Justice Scalia, writing for Court, acknowledged the inexact contours of the provision, but stated 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,” and 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 FDCA.” Slip Opinion at 8. The Court completely dismissed any notion that the phase of the research in which information is developed can be a basis for denial of the exemption. Slip Opinion at 9.

In addressing the Federal Circuit’s determination that the exemption does not globally embrace all experimental activity that might lead to an FDA submission, the Supreme Court agreed 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.” Slip opinion at 12.

Here, the Supreme Court noted the concern expressed by the Federal Circuit that a limited construction of §271(e)(1) is necessary to preserve rights in patents to “research tools”, where the primary market, if not the only market, is often pharmaceutical companies and other researchers engaged in research where the information developed may be used in FDA submissions. Because the parties never argued, and the record did not show, that the Integra patents covered research tools, the Supreme Court declined to “express a view about whether, or to what extent, §271(e)(1) exempts from infringement the use of ‘research tools’ in the development of information for the regulatory process.” Slip Opinion at 12, n.7.

The Supreme Court departed from its agreement with the Federal Circuit’s concern for the global embrace of the research exemption, however, when it stated that “under certain circumstances” the exemption is sufficiently broad to protect the use of patented compounds in situations where there is “experimentation on drugs that are not ultimately the subject of an FDA submission” or where there is “use of patented compounds in experiments that are not

ultimately submitted to the FDA.” Slip Opinion at 12.

Justice Scalia observed that the Federal Circuit’s narrow reading of the phrase “*solely* for uses reasonably related to clinical testing for FDA” to exclude from the exemption research used to identify the best candidate drugs disregards the reality that research is a trial and error process, particularly at the preclinical stage of drug approval. “Properly construed, §271(e)(1) leaves adequate space for experimentation and failure on the road to regulatory approval: 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, would be appropriate to include in a submission to the FDA, that use is ‘reasonably related’ to the ‘development and submission of information’ under the FDCA. Slip Opinion at 13-14.

While the Supreme Court’s decision clearly opens the exemption under §271(e)(1) to research developed during all stages of the regulatory process, the latter statement by the Court, as well as others throughout the opinion, suggest that questions such as the intent of the researcher, his or her belief that the patented invention may work, and whether or not the researcher had a particular biological process and a particular physiological effect in mind, although not stated in Section 271(e)(1), are relevant in determining whether or not the research qualifies for the exemption.

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