

The Value of 'Research Tool' Patents in View of *Integra v. Merck*

By Deborah A. Somerville, Jeffrey Ginsberg and K. Patrick Herman

On June 6, 2003, the Court of Appeals for the Federal Circuit seemingly breathed new life into research tool patents when it held that the use of patented peptides for drug discovery was not exempt from infringement under the "safe harbor" provision of 35 U.S.C. §271(e)(1). *Integra Lifesciences, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003). In an earlier case, *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833, 2001 WL 1512597 (S.D.N.Y. 2001), a district court had ruled that the use of patented intermediates for drug screening was non-infringing, thereby implicating that the use of other research tool patents for drug discovery was likewise sheltered from infringement liability under §271(e)(1).

The *Bristol-Myers* district court decision had raised questions in the industry about the value and enforceability of research tool patents. The Federal Circuit's decision in *Integra* provides patentees with some indication that their patents can be enforced against at least pre-clinical drug discovery uses of the research tools.

However, in resurrecting research tool patents, the Federal Circuit determined that the jury's reasonable royalty damages award of \$15 million was not supported by the evidence and remanded for further considerations. Accordingly, in deciding whether to

litigate or license research tool patents (or to pursue patent protection in the first instance), patent owners and research tool users will want to carefully consider the value of the particular research tool patents at issue. This article reviews the *Integra* decision and its background, and outlines various factors that might be evaluated to provide an answer.

THE HATCH-WAXMAN ACT PROVIDED A 'SAFE HARBOR' AGAINST PATENT INFRINGEMENT

The general infringement section of the patent code, 35 U.S.C. §271(a), broadly stipulates that "making, using, selling, offering to sell, or importing" into the United States any "patented invention" constitutes patent infringement. While this provision encompasses a wide range of activities, an exemption was created in 1984 by the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (the "Hatch-Waxman Act").

The Hatch-Waxman Act, which attempted to balance the public's need for generic drugs and the rights of patent holders, added 35 U.S.C. §271(e)(1), *inter alia*, to the patent code. This section states that "it shall not be an act of infringement to make, use, ... or sell ... a patented invention ... solely for uses reasonably related to the development and submission of information" to the Food and Drug Administration (FDA). Hence, §271(e)(1) effectively provided a "safe harbor" for generic drug manufacturers engaged in conducting experiments required for regulatory approval of a

generic substitute. As such, it served the legislative purpose of facilitating access to generic versions of marketed drugs soon after the drug patent expired. H.R. Rep. No. 98-857, pt. 2, at 6 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2686, 2692.

A series of subsequent court cases have outlined the contours of the §271(e)(1) safe harbor exemption. The courts, for example, have concluded that it applies to *all* "patented inventions," including "medical devices" and "human biologics" (which do not as yet have generic equivalents) as well as "drug" products. *See, e.g., Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990); *Amgen, Inc. v. Chugai Pharm. Co.*, 13 U.S.P.Q.2d 1737, 1779-80 (D. Mass. 1989). The "reasonably related" language of §271(e)(1) has also been interpreted more broadly than implied by the legislative history to cover a range of activities having purposes beyond just FDA approval, such as trade show demonstrations and the distribution of clinical data to parties besides the FDA. *See, e.g., Teletronics Pacing Systems, Inc. v. Ventritex*, 982 F.2d 1520, 1524, 1526 (Fed. Cir. 1992).

BRISTOL-MYERS EXPANDED THE SAFE HARBOR TO COVER DRUG DISCOVERY ACTIVITIES

In *Bristol-Myers*, the district court concluded that the use of patented intermediates in an attempt to identify new drugs was "reasonably related" to the development of information for the FDA and therefore protected by the §271(e)(1) safe harbor. In doing so, the *Bristol-Myers* district court stated that it applied the same legal standard

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concerning “reasonably related” uses as had been affirmed previously by the Federal Circuit, namely, whether there is a “decent prospect that the ‘use’ in question would contribute (relatively directly) to the generation of information” relevant to FDA approval. *Bristol-Myers*, 2001 WL 1512597, at *3-4 (citing *Intermedics, Inc. v. Ventritex, Inc.*, 775 F.Supp. 1269, 1280 (N.D. Cal. 1991)).

The district court recognized that the experimental work at issue might not actually be submitted to the FDA or lead to any actual FDA submissions. Nonetheless, applying the *Intermedics* standard, the district court concluded that there was a “decent prospect” that the work — which provided the “first steps in creating a record that may be submitted to the FDA” — would “contribute (relatively directly) to the generation of information” relevant to the FDA. *Id.* at *5-6. The court reasoned that a different conclusion might preclude the parties from ever engaging in the experimentation required to identify lead candidates for FDA submission. *Id.* at *6-7.

The district court’s interpretation of §271(e)(1), extending the safe harbor to the use of patented inventions in new drug identification experiments, was not challenged on appeal. See *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 326 F.3d 1226 (Fed. Cir. 2003). As a result, the Federal Circuit did not have an opportunity to refine its earlier interpretations of §271(e)(1) in light of the district court’s holding. In the meantime, the *Bristol-Myers* decision provided a basis for arguing that uses of research tool patents by other parties for drug discovery were also exempt from infringement under the §271(e)(1) safe harbor.

THE FEDERAL CIRCUIT RESURRECTED RESEARCH TOOL PATENTS IN INTEGRA

In *Integra*, the Federal Circuit had the opportunity to determine whether pre-clinical drug screening uses of research tool patents are exempt from infringement under the §271(e)(1) safe harbor. The court found that, under such circumstances before

it, such early-stage drug discovery activities were not protected and remanded for further consideration of a reasonable royalty award for infringement damages.

THE LOWER COURT DECISION

In the district court, *Integra* asserted that Merck (in collaboration with The Scripps Research Institute) infringed five patents on peptides containing certain sequences by using the claimed peptides to identify potential drug candidates. Merck argued that its

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screening activities were exempt under the §271(e)(1) safe harbor because they were “reasonably related” to the submission of information to the FDA.

A jury determined that Merck infringed *Integra*’s patents (as construed by the district court) and awarded \$15 million in reasonable royalty damages. *Integra*, 331 F.3d at 862. The district court entered this verdict after finding that the safe harbor exemption of §271(e)(1) did not apply to Merck’s activities. *Id.*

THE FEDERAL CIRCUIT’S LIMITATION OF THE SAFE HARBOR

In a majority opinion written by Judge Rader, the court began its consideration of Merck’s claim for protection under the safe harbor by noting that the actual language of §271(e)(1) “strictly limits the exemption ‘solely’ to uses with a reasonable relationship to FDA procedures.” *Id.* at 866. Thus, the safe harbor exemption is not unbounded. The court then turned to the legislative history of §271(e)(1), and

observed that the safe harbor exemption was designed to permit a limited amount of pre-market approval testing by generic manufacturers “to facilitate the immediate entry of safe, effective generic drugs into the marketplace upon expiration of a pioneer drug patent.” *Id.* at 866-67. The court also stated that the “FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval.” *Id.* at 866.

With this context in mind, the court concluded that activities that do not directly produce information relevant to the FDA fall outside the scope of the exemption. *Id.* at 867. The exemption does not extend to “exploratory research that may rationally form a predicate for future FDA clinical tests” since the FDA has no interest in such information. *Id.* Hence, Merck’s pre-clinical research, which did not supply information for submission to the FDA, but identified the best drug candidate to subject to future clinical tests, was not protected by the safe harbor.

The court justified its holding by pointing out that a contrary expansion of the safe harbor would not confine its scope “to de minimis encroachment” on the patentee’s rights. *Id.* The court also recognized that a primary benefit of research tools, particularly in the biotech arena, is to facilitate general research to identify drugs, and that expanding §271(e)(1) to encompass Merck’s screening activities would “effectively vitiate the exclusive rights of patentees owning biotechnology tool patents.” *Id.* Moreover, “exaggerating §271(e)(1) out of context would swallow the whole benefit of the Patent Act for some categories of biotechnological inventions.” *Id.*

Judge Newman wrote a dissenting opinion that focused on both the applicability of the common law research exemption (which the majority noted was not before the court) and the safe harbor exemption of §271(e)(1). The dissent stated that the patent system is designed to facilitate technical advance by requiring disclosure by the patentee in exchange for the protections provided. *Id.* at 873. (Newman, J., dissenting). Thus, the subject matter of a patent

“may be studied in order to understand it, or to improve upon it, or to find a new use for it, or to modify or ‘design around’ it.” *Id.* at 875. The dissent acknowledged that the research exemption has limits but did not define them because, it asserted, if Merck’s activities fell outside the scope of the research exemption they are protected by §271(e)(1).

THE FEDERAL CIRCUIT’S REMAND ON DAMAGES

In reviewing the jury’s award of \$15 million in reasonable royalty damages, the Federal Circuit noted that the patent code states that “upon finding for the claimant the court shall award ... damages adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use ... of the invention.” 35 U.S.C. §284. Thus, an injured patentee is entitled to at least a reasonable royalty, even when unable to show an established royalty rate or lost profits (which may be particularly hard to prove for infringement of a research tool patent, since the patentee will often find it difficult to show that “but for the infringement, customers likely would have purchased the patentee’s product rather than turning to a ... non-infringing alternative.” Donald Ware, *Research Tool Patents: Judicial Remedies*, 30 AIPLA Q.J. 267, 277 (2002).

The Federal Circuit acknowledged that determining the amount of a reasonable royalty may be especially problematic for research tool patents. Thus, the majority set forth a number of factors which may be considered to determine the amount of a reasonable royalty, many of which are also detailed in the Ware article (referenced in the court’s opinion). *Integra*, 331 F.3d at 871.

The majority began its damage analysis by emphasizing that “a reasonable royalty calculation envisions and ascertains the results of a hypothetical negotiation between the patentee and the infringer at a time before the infringing activity began.” *Id.* at 869. The court noted that the time of this hypothetical negotiation can be

important because risks, along with the value of the hypothetical license, can change significantly over time, particularly in such rapidly developing fields as the biotechnology arts. *Id.* at 870. Thus, if an infringer would have been unable to predict the success of a final product while still in a pre-clinical stage, the appropriate reasonable royalty may be lower than where success is more assured.

At the same time, the court recognized that the nature of the research tool patent itself can bear on the magnitude of the reasonable royalty award. For example, some tools, especially those that enable “the identification of a drug candidate during high throughput screening ... may supply more value to the ultimate invention than a research tool used to confirm an already recognized drug candidate’s safety or efficacy.” *Id.* at 871.

In addition, once the proper date for the hypothetical license negotiation has been determined, a court can inform its reasonable royalty determination by looking at other, similar licenses. *Id.* at 870-71. The majority noted that license comparisons are inherently suspect and should be made carefully because scientific and economic risks can be very different from license to license. *Id.*

The majority also stated that the number of licenses an infringer would have had to obtain to develop a drug without infringing a patent is also relevant to the reasonable royalty determination. *Id.* at 871. Such royalty stacking can result in a monumental award, especially if reach-through royalties are determined to be appropriate. *Id.* A court cannot award a reasonable royalty that the infringer would have been unwilling to pay.

FUTURE CONSIDERATIONS AND PRACTICE POINTERS

By refusing to expand the §271(e)(1) safe harbor to cover early-stage drug discovery, the Federal Circuit’s decision in *Integra* provides patentees with some assurance that their research tool patents can be enforced against at least pre-clinical discovery uses. Confronted

with this limitation, prospective users of the research tools may opt to take a license or pursue design-arounds.

Possible *en banc* review by the Federal Circuit and future decisions may refine the *Integra* decision. Savvy parties will stay tuned for further developments. In the meantime (and in any event), patentees will want to seek protection for the end products identified by the research tools, to the extent possible in view of the prior art.

Further, in deciding whether to litigate or license, the patentee and prospective licensee will want to weigh carefully the possible damages, as measured by at least a “reasonable royalty” in view of the costs and benefits (tangible and intangible) of litigation. The Federal Circuit’s decision in *Integra* provides guidance as to the appropriate factors to consider when confronting this issue. These factors include: the time of the hypothetical negotiation or infringement and the parties’ perceived risks and benefits at that time; the nature of the patented research tool, which can include where it will be used in the drug discovery continuum (*ie*, for identifying new drugs or for testing the safety or activity of a selected drug product), as well as the uniqueness of the patented research tool and whether there are non-infringing alternatives; the existence of other similar licenses; the likelihood of royalty stacking; and the possibility of reach-through royalties (implicitly approved by the Federal Circuit’s discussion), particularly where the patented research tool provides a new way of providing an end product. The nature of the parties’ businesses and the commercial realities of the marketplace should, of course, also be considered.



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