

# Research Tool Patents: Have Reports of Their Death Been Greatly Exaggerated?

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## Introduction

Judge Pauline Newman of the Court of Appeals for the Federal Circuit characterized a research tool as “a product or method whose purpose is use in the conduct of research, whether the tool is an analytical balance, an assay kit, a laser device (*citation omitted*), or a biochemical method such as the PCR (polymerase chain reaction). It is as subject to the patent right as is any other device or method, whether it is used to conduct research or for any other purpose.<sup>1</sup>”

Research tool patents are a mainstay of many life science companies. In fact, some companies center their entire business plans around the use or sale of particular research tools. The value of research tools in life science research is unquestionably high; however, recent developments in patent law and tightening budgets have forced companies and universities to decide whether to devote precious resources to drafting and prosecuting research tool patents. The purpose of this article is to set out the current state of the law and discuss whether it makes sense to attempt to obtain and enforce research tool patents.

## Legal Considerations

### The Hatch-Waxman Act

The United States’ patent system is founded on a basic quid pro quo: Rather than keeping an invention secret, if an inventor agrees to provide the public with a description of his or her novel and nonobvious invention that is sufficient to permit those skilled in the art to make and use the invention then the inventor will be granted a 20-year monopoly right on the use of that invention. The extent of this monopoly right is limited to the right to exclude others from making, using, selling, or offering for sale the patented invention. This right to exclude, however, does not come without exceptions.

One such exception is found in the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act.<sup>2</sup> The Hatch-Waxman Act includes provisions designed to remedy two unintended problems with the patent system experienced by companies developing products that are subject to U.S. Food and Drug Administration (FDA) approval.<sup>3</sup> The first problem was a shortening of the effective life of a patent caused by the extended premarket regulatory approval period required for many products.

For example, most companies developing therapeutic products will file for patent protection very early in the development process, typically well before clinical trials begin. As a result, the 20-year term of the patent is ticking away while the product is in clinical trials or awaiting FDA approval. Often therapeutic products have as little as 5 to 10 years of patent life remaining at the time of market approval. To remedy this first problem Congress allowed companies to regain a certain percentage of the time spent gaining regulatory approval in the form of a patent term extension on a single patent covering the approved product (or method of using the approved product).

The second problem addressed by the Hatch-Waxman Act occurred at the opposite end of the patent lifecycle. While innovator companies were losing early portions of their patent term because of the regulatory process, they were gaining effective patent protection beyond the end of the patent's life. For example, if a company wanted to market a generic version of a patented drug, it had to wait until the patents covering the drug (or methods of using the drug) expired before initiating the development process or be subject to a lawsuit for patent infringement.<sup>4</sup>

Even for a generic drug, which does not require full-fledged clinical trials, the development and regulatory process takes years. This period during which the generic manufacturer was gaining regulatory approval was a de-facto extension of the patent holder's monopoly right. Congress attempted to remedy this problem with the passage of 35 U.S.C. § 271(e)(1) (271(e)(1)), which states that it is *not* 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."<sup>5</sup> This allows generic manufacturers to initiate clinical test-

ing prior to the expiration of the patents without the fear of an infringement suit. It is this exception to a patent holder's right to exclude that presents potential issues for the owners of research tool patents.

### 35 U.S.C. § 271(e)(1)

According to 271(e)(1), any use of a "patented product" that is "reasonably related" to the development of data to be submitted to the FDA does not infringe a patent claiming the product. This exception has been interpreted to extend to all products subject to FDA approval, including medical devices.<sup>6</sup>

The Supreme Court assessed the scope of activities that are reasonably related in *Merck v. Integra*.<sup>7</sup> The Court concluded that the exception from infringement covers activity by a drug maker if the drug maker 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. The Court explicitly noted that the issue of whether the exception from infringement applied to research tool patents was not before the court.<sup>8</sup>

The decision in *Merck v. Integra* unleashed a storm of speculation as to whether patents to research tools would now fall under the exception to infringement. Many commentators speculated that the broad language used in the Supreme Court's decision (and the underlying Federal Circuit decision) signaled that the courts would find that using patented research tools to generate data to be submitted to the FDA would be exempt from claims of patent infringement under 271(e)(1).<sup>9</sup>

This question is immensely important to the life science industry because research tools are such an integral part of many companies' businesses. For example, assume that Company A is a pharmaceutical company developing novel compounds that activate the XYZ receptor. Company B has a patented method for screening compound libraries for their ability to activate to the XYZ receptor, which allows the development process to be shortened by 50 percent.

Company B's business is built on providing services using its patented method. If research tools are exempt from patent infringement, then Company A is free to implement Company B's patented method without obtaining a license or paying a royalty and without Company B's consent. Effectively, Company B is out of business. Many scenarios such as this can be (and have been) hypothesized.

Unfortunately, neither the Supreme Court nor the Federal Circuit offered much guidance on the issue, leaving the life science community to speculate as to the enforceability of research tool patents.

### ***Proveris v. InnovaSystems***

In August 2008 the Federal Circuit provided some limited guidance into the question.<sup>10</sup> Proveris Scientific Corp. owns a patent claiming an apparatus for characterizing aerosol sprays commonly used in various drug-delivery devices, such as nasal spray pumps and inhalers. Data generated by this device was required to be submitted to the FDA in order for companies to gain approval for certain inhaler-based drug-delivery systems. The product was marketed to drug manufacturers and the FDA as a tool solely useful in generating data for the FDA approval process, but the patented device itself was not subject to FDA approval.

InnovaSystems made and sold a similar product. Proveris sued InnovaSystems alleging infringement of its patents. InnovaSystems claimed that the product was exempt from infringement under 271(e)(1) because it generated data that was reasonably related to the generation of data that would be submitted to the FDA. The Federal Circuit disagreed with InnovaSystems.

The court essentially found that the problems intended to be remedied by the Hatch-Waxman Act did not affect the makers of products that were not subject to the FDA approval process, so they shouldn't be entitled to the benefits. The court stated:

*Because Proveris' patented product is not subject to a required FDCA<sup>11</sup> approval process, it is not eligible for the*

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*benefit of the patent term extension afforded by 35 U.S.C. § 156(f). At the same time, because Innova's OSA device also is not subject to a required FDCA approval process, it does not need the safe harbor protection afforded by 35 U.S.C. § 271(e)(1).<sup>12</sup>*

The court's decision in *Proveris* appears to set up a simple if/then test to determine whether a product is a patented invention under 271(e)(1). If the product is not subject to FDA approval, then infringers of patents covering those products are not exempt from claims of infringement under 271(e)(1).

### *Proveris and the Future of Research Tool Patents*

On its face, the *Proveris* decision seems to be good news for those that develop or market research tools. Since the vast majority of research tools are not subject to FDA approval, it would appear that infringers of patents claiming research tools are not entitled to hide behind 271(e)(1). If this is true, then those patent holders can effectively sue to stop infringement of these patents. Also, the value of research tool patents are significantly increased since licenses to these patents may be needed by a significant number of companies using the patented tools. However, many research tools may also have uses as therapeutics, which complicates the analysis.

For example, assume that researchers at the University of Neverland have developed and patented a new cell line. The cell line can be used to screen for molecules having a desirable characteristic, such as the ability to inhibit cell de-differentiation making it a potentially valuable research tool. Further, assume that the cell line can also be used as a cell therapeutic for Parkinson's disease.

Bigpharma learns of the new cell line developed at the University of Neverland and decides to use it to screen its small molecule library for lead compounds for development. Is this activity exempt from infringement?

It is not necessary to obtain premarket approval from the FDA to screen small molecules or sell products for screening small molecules for a given activity. Accordingly, Bigpharma

is not hurt by the regulatory requirements for clinical testing that might delay entry of their product into the market. Since it is not hurt by the regulatory requirements, Congress did not intend for it to be benefited by the Hatch-Waxman Act. Therefore, Bigpharma is not entitled to the exemption from infringement provided by the Hatch-Waxman Act, and using Neverland's cell line for screening is an infringement.

Now consider the case where Bigpharma decides to use the cell line to develop a therapeutic product.<sup>13</sup> Now it is necessary to obtain premarket approval from the FDA to use the new cell line as a therapeutic. Accordingly, Bigpharma is hurt by the regulatory requirements for clinical testing that will delay entry of its product into the market. Since it is hurt by the regulatory requirements, the allegedly infringing activity is within the class of activities Congress intended to be addressed by the Hatch-Waxman Act. Therefore, it is entitled to the exemption from infringement provided by the Hatch-Waxman Act and this use of the cell line is not an infringement.

In addition to cell lines, similar problems can be envisioned with other research tools that can also be used as therapeutics. These may include antibodies that can be used for diagnostic or research purposes and as a therapeutic agent. The same can be said for nucleotides, which can be used as gene therapy agents as well as research tools. Even chromatography resins, which obviously are primarily used in laboratory research and manufacturing, have been used as therapeutic agents as metal chelators.

As is demonstrated by the preceding analysis, sometimes one use of a technology may be exempt from patent infringement, while other uses of the same technology may not. But, does this matter from a technology transfer perspective?

In the case of the clear use of a technology as a research tool a potential user will have to take a license or be subject to a claim of patent infringement since it is outside of the protection provided by the Hatch-Waxman exception. Thus, it makes sense for the University of Neverland to commit the resources to obtaining a patent with claims covering the technology. In this situation patenting inventions that are pure research tools (i.e., that have no therapeutic potential), is still a viable option. In fact, failure to protect these technology could result in significant loss of potential revenue.

In the situation where the technology is used as a therapeutic agent, even though the potential infringer's initial activities fall within the Hatch-Waxman exemption and are not subject to an infringement suit, the university should still consider investing in the patenting of the therapeutic technology. Bigpharma will still likely be required to license the technology assuming the initial evaluation is positive.

Even though the early development work may be performed without the risk of patent infringement, as soon as the company markets the product it will emerge from the protection of 271(e)(1) and will be subject to a patent infringement suit. As such, it is very unlikely that a company would elect to develop the technology without a license. Thus, even in the case where some uses of a patented product may be immune from infringement suit, it still makes sense for the university to obtain patent protection.

## Conclusion

After the Supreme Court's decision in the *Integra* case, there was significant concern in the life sciences community that the use of research tools may be exempted from infringement by 271(e)(1), leaving many biotechnology and service organizations with no recourse against infringers. Some commentators predicted dire consequences for large sectors of the life science industry. The recent *Proveris* case appears to signal that 271(e)(1) will not exempt the use of research tools that do not require FDA approval from patent infringement claims.

Moreover, even though the initial use of some research tool patents may be exempt from an infringement suit, such patents will likely have value because of their later commercial potential. As a result, research tool patents should become much more attractive to technology transfer offices, entrepreneurs, and development partners. Reports of the death of the research tool patent have been greatly exaggerated.

*For more information on research tools, see "Research Tools Policies and Practices: Perspective of a Public Institution," by Uri Reichman, PhD, MBA; Susan E. Ano, PhD; and Steven M. Ferguson, MBA, CLP, in the 3rd Edition of the AUTM Technology Transfer Practice Manual.*

## Notes

1. *Integra v. Merck*, 331 F.3d 860, 878 (Fed. Cir. 2003), reversed by *Merck v. Integra*, 545 U.S. 193 (2007).
2. Pub. L. No. 98-417, 98 Stat. 1585 (1984), codified at 21 U.S.C. §§ 355, 360cc (2000), and 35 U.S.C. §§ 156, 271, 282 (2000).
3. It is generally recognized that the Hatch-Waxman Act was intended to address problems in the development of therapeutic products and generic versions of those products, but subsequent decisions have expanded the scope of the statutes beyond therapeutics. (See e.g., *Eli Lilly & Co v. Medtronic, Inc.*, 496 US 661 (1990)).
4. Recall that unlike many other countries, the United States does not recognize a research exemption to patent infringement. (For example, see *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002)).
5. 35 USC § 271(e)(1). The Hatch-Waxman Act also sets out a legal framework that is designed to speed up the introduction of generic drugs by giving generic manufacturers an incentive to challenge patents covering brand name drugs. The first to file an abbreviated new drug application is awarded a six-month period to exclusively market the generic drug.
6. *Eli Lilly & Co v. Medtronic, Inc.*, 496 US 661 (1990), see also *AbTox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997). Note that there is some question whether 271(e)(1) covers products that are not eligible for patent term extension under 35 USC § 156, but the *AbTox* case seems to suggest that all products subject to FDA approval are considered “patented products” for the purposes of 271(e)(1). (See also, *Proveris Scientific Corp. v. InnovaSystems, Inc.*, Federal Circuit docket no. 2007-1428, decided August 5, 2008.)
7. *Merck KGAA v. Integra Lifesciences I, LTD*, 545 US 193 (2005).
8. *Id.* FN 7.
9. See, for example, Wolrad Prinz zu Waldeck und Pyrmont, 14 *Mich. Telecomm. Tech. L. Rev.* 367 (2008), Paul Wiegel, *Boston College Intellectual Property & Technology Forum*, November 29, 2007.
10. *Proveris Scientific Corp. v. InnovaSystems, Inc.*, 2008 WL 2967100, Federal Circuit docket no. 2007-1428, decided August 5, 2008.

11. Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, ch. 675, 52 Stat. 1040 (1938) (codified at scattered sections of title 21 of the United States Code).
12. *Proveris* at page 16.
13. This analysis assumes that the activity is “reasonably related” to developing information for submission to the FDA for approval. The scope of activity that is “reasonably related” was addressed in *Integra* and a detailed discussion of what activities meet this definition is beyond the scope of this paper.