

The Value of Research Tool Patents

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Recent legal controversies have led to uncertainty regarding the value of research tools and patents covering them. In particular, the U.S. Supreme Court's *Merck v. Integra* decision has broadened the safe harbor exemption for patented inventions used in drug testing, but it failed to leave a clear view of just how far back into the research and development process the exemption extends. The exemption was formerly seen as limited to the clinical studies that directly generate data for submission to the U.S. Food and Drug Administration (FDA). But now, owners and licensees of research tool patents are asking themselves what their patents are worth in the new legal landscape.

What exactly is a research tool? A narrow view would limit research tools to instrumentation, assay reagents, screening libraries, basic assay methods (e.g., PCR), computer software, and similar materials that are broadly applicable to any scientific research. A broader view would also encompass drug targets (e.g., transgenic animals, cells, receptors, enzymes, genes), candidate drugs, and possibly even patented therapeutic or diagnostic agents, whose use might be part of the discovery process for a new drug or diagnostic agent. The real key to whether a substance or a method is a research tool is how it is used, namely, whether it is used in research. Adopting a narrower definition of research tools is generally not useful, because the same object can be either a research tool or not, depending on how it is used. For example, an antibody can be used as a therapeutic drug (not a research tool), or it can be a component of an assay kit used in the earliest stages of drug research (clearly a research tool).

In certain limited circumstances, the use of patented technology in research can fall within the so-called common law research exemption, under which an otherwise infringing use of a patented composition, device, or method is allowed. The research exemption traces its roots back through nearly 200 years of U.S. court decisions, and it was recently refocused in *Madey v. Duke University*. In *Madey*, the Court of Appeals for the Federal Circuit held that the exemption is limited to the use of a patent for philosophical or scientific inquiry, and made clear that research may not be immune from patent infringement if it has "the slightest commercial implication" or if it furthers the business objectives of the entity using the technology. *Madey* thereby narrowed the research exemption and made clear that research with even minimal commercial implication, including research during the early stages of drug development, may not be eligible for the long-established infringement exemption. Thus, *Madey* has strengthened research tool patents.

Following *Madey*, the U.S. Supreme Court in *Integra v. Merck* evaluated the scope of another statute-based research exemption. In that case, Merck had used Integra's patented RGD peptides during pre-clinical work, while screening a handful of compounds (cyclic RGD peptides) for their ability to inhibit tumor growth. The screened compounds included the one which later was selected for clinical trials. It was generally accepted that the use of the RGD peptides during *clinical* work for FDA approval was exempt from infringement under the statutory safe harbor of 35 U.S.C. § 271(e)(1), which exempts otherwise infringing activities from liability if those activities are "solely for uses reasonably related to development and submission of information [to the FDA for drug approval]". The issue was whether the infringement of a patent during *pre-clinical* (pre-IND) work also qualifies for the safe harbor

exemption of 35 U.S.C. § 271(e)(1).

The U.S. Supreme Court held that for work to be “reasonably related” to submission of information to FDA, the work did not have to produce results that were ultimately submitted to FDA, and did not have to be performed exclusively on the compound brought to clinic. The Court provided some guidance as to what experiments fall within the safe harbor, though certainly not a bright-line test. “Properly construed, § 271(e)(1) leaves adequate space for experimentation and failure on the road to regulatory approval: At least where a 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, that use is reasonably related to the development and submission of information under . . . § 271(e)(1).”

So, where does that leave research tools? In *Merck*, the Supreme Court dealt with the use of patented compounds which were themselves candidate drugs, and strictly speaking its holding only applies to the use of patented compounds which later become the focus of clinical testing for FDA requirements, or a few related compounds that do not continue in the clinic. However, the Supreme Court specifically stated that the Integra RGD peptides clearly were not research tools, and specifically declined to express a view on “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.” It appears for now that the Supreme Court has left open the possibility that any research tool (*i.e.*, something used in research, but not the object of study itself) may be within the § 271(e)(1) safe harbor infringement exemption. If the Court were to apply the same logic that is applied to patented drug candidates, the use of a research tool would be exempt from infringement if it is used in clinical or preclinical research to test a compound for which: (1) there is a reasonable basis for believing that the compound may work, by way of a particular biological process, to produce a particular physiological effect; and (2) the results, if successful, would be appropriate for submission to the FDA.

Thus, by the Supreme Court’s *Merck* decision, the scope of the § 271(e)(1) safe harbor infringement exemption has been enlarged somewhat to include certain preclinical research. Clearly, however, the safe harbor does not extend all the way back to the initial screening experiments to identify an initial set of drug candidates, or to basic research to uncover fundamental pharmacological mechanisms where no specific candidate exists. Research tools that are used primarily for such activities are as valuable today as ever. These would include most drug targets, basic molecular biological and immunological techniques, reagents, instruments, and components and methods for screening. On the other hand, research tools which are primarily useful in the later stages of characterizing a small number of drug candidates and identifying the final candidate, or in preparing pre-IND safety or pharmacokinetic data, may have declined in value since *Merck v. Integra*.

A further recent development relevant even to early stage research tools is *Bayer v. Housey Pharmaceuticals*. In the *Bayer* case, the issue was whether the importation of data, *e.g.*, screening results, from outside the U.S. is blocked by 35 U.S.C. § 271(g), which makes it an act of infringement to import a product made by a process patented in the U.S., unless the product has been materially changed. In *Bayer*, the Federal Circuit held that § 271(g) applies only to importation of material objects, not data. As a result of this decision, the value of research tools

used in early stage research, such as screening systems, has in principle been reduced to the nuisance value of having the work performed overseas in a patent-free zone, i.e. in a country where the research tool has not been patented. This underscores the value of worldwide patent protection for important early stage research tools.

The monetary value of research tools depends on where along the drug development timeline they can be used. Earlier stage tools are generally more valuable because they are less at risk of falling within the § 271(e)(1) infringement exemption, although if they only result in the generation of data, and no material product, their value also can be limited by the *Bayer* holding. Another factor of course in the value of a particular research tool is the ultimate commercial value of the kind of drug that can be discovered using the tool. The more valuable the drug, the more valuable the tool.

Recovering damages for infringement of research tool patents can be tricky. First, a kind of “informal research exemption” has been practiced by some pharmaceutical companies, who sometimes opt not to take a license, reasoning that they can take the license later if the product becomes commercially important; alternatively, they may try to invalidate the tool patent, or simply claim the § 271(e)(1) safe harbor exemption. Discovering infringement during early stage, highly confidential pharmaceutical research also can be difficult in certain circumstances.

While several recent legal decisions impact the value of certain research tools, overall their value has not changed significantly. For the future, some speculate that the drive to contain costs for developing pioneer drugs may motivate the expansion of the § 271(e)(1) infringement exemption. On the other, a strong research tools industry is vital for feeding the discovery pipeline, and if the value of research tools is eroded by expansion of the § 271(e)(1) exemption, there will eventually be a negative impact on the discovery of new drugs.